

ABSTRACT

PROBERT, CHANDLER AUSTIN. Investigating Polycyclic Aromatic Hydrocarbon Dermal Absorption in Firefighters and the Efficacy of Decontamination Wipes. (Under the direction of Dr. R. Bryan Ormond and Dr. Ronald Baynes).

In their line of work, firefighters are exposed to thermal and chemical hazards far more frequently than their first responder counterparts. Several health studies conducted on firefighters have identified that firefighters have increased risk and incidence of multiple types of cancers. During the summer of 2022 the International Agency for Research on Cancer (IARC) declared occupational firefighting as a class 1 carcinogen, meaning it is a known carcinogen based on “sufficient evidence”. As a result, firefighters and researchers are increasing their efforts to study and understand firefighter and fire investigator chemical exposures.

One group of chemicals that firefighters are routinely exposed to are polycyclic aromatic hydrocarbons (PAHs). Within the class of PAH compounds the environmental protection agency has identified 16 priority compounds based on their environmental abundance, risk of exposure, and carcinogenicity. Numerous studies have researched PAH concentrations in various fire scenarios, such as live burns, training burns, shipping container burns, etc. Furthermore, these PAH compounds have been found in high concentrations in the air during fire response and overhaul phase. Furthermore, these chemicals have been repeatedly found on the gear and skin of firefighters after fire response.

Firefighters are exposed to fireground contaminants, such as PAHs, through ingestion, inhalation, and dermal absorption. Through standard operating procedures and mitigation strategies, exposure through ingestion and inhalation can be greatly reduced, leaving dermal absorption a primary route of exposure for firefighters. This research aims to study the dermal absorption of three PAHs, naphthalene, phenanthrene, and benzo[a]pyrene and the effects the fireground (increased temperatures) and on-scene decontamination (use of decontamination wipes) has on dermal absorption. Furthermore, multiple decontamination wipe products will be tested for the effectiveness at removing PAHs from the skin using a synthetic skin model.

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Investigating Polycyclic Aromatic Hydrocarbon Dermal Absorption in Firefighters and the
Efficacy of Decontamination Wipes

by

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DEDICATION

I would like to dedicate this to all the brave men and women first responders. It takes a great amount of courage and selflessness to put the safety of a stranger before your own. It has been an honor to make the acquaintance of so many brave individuals who I have had the pleasure of working with during my time as a graduate researcher. To those who have perished in the line of duty or lost the battle against cancer your memories will live on in the hearts of your families, the lives you have touched in your communities, and those who understand the severity of your sacrifice. Thank you.

BIOGRAPHY

Chandler is a naturally curious individual with several interests and passions. When he finds a topic that interests him it quickly becomes his new obsession. Outside his primary research areas of chemical exposure assessment, toxicology, textile engineering, and analytical chemistry Chandler enjoys learning about photography and videography, personal finance and business, real estate, weightlifting, and nutrition.

Chandler first stepped on the famous red bricks of North Carolina State University back in the fall of 2014 and in that moment, he knew that he had found a new place to call home. After applying to the Polymer and Color Chemistry program because it sounded “interesting,” Chandler started his journey of becoming a scientist. When searching for an area of research to pursue Chandler discovered the Textile Protection and Comfort Center, also known as TPACC. He decided to volunteer to learn more about what research TPACC was involved in and learned about protective textiles and personal protective equipment. After getting the opportunity to go into the field to see the importance of TPACC’s research Chandler decided he would focus his efforts towards helping improve the lives of those who work in dangerous occupations.

Chandler has obtained his baccalaureate degree in Polymer and Color Chemistry, his master’s degree in Textile Engineering, and now his Doctor of Philosophy degree in Fiber and Polymer Science. Some of his fondest memories include going out to eat lunch with his lab group on Fridays, playing foosball, MIST testing, late nights at the NC State Vet School, and watching firefighters set abandoned structures ablaze. As his time at NC State has come to an end, Chandler looks forward to his next step in his career.

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Over the course of my many, many years at NC State I have met so many people who I can call a friend. Individuals who lifted my spirits when I was having a bad day, took me under their wing and mentored me, or gifted me a memory that I will never forget, whether they realize it or not. With that said, there are a handful of people I would like to acknowledge and express my gratitude.

Before I can acknowledge others for their guidance and help, I would like to first acknowledge my personal achievement. I am the first in my family to obtain a Doctoral degree. Graduate school is not for everyone, it is extremely challenging, something I learned time and time again. I am glad to have persevered and see it through to the end, even though it felt like I may never reach my goal. Nobody will ever know of the long nights in the lab or the countless hours I spent writing in the library. I am proud of the contribution my work will make to improve the health and safety of firefighters and fire investigators.

The first of my acknowledgements would be my family. To my mother, Margie, my father, Charlie, and my two younger brothers, Kyle, and Clayton, thank you for all your support.

I would also like to thank Dr. Bryan Ormond, my advisor, mentor, and friend. Bryan thank you for seeing the potential in me when I was an undergrad and wasn't sure about what I wanted to do. Your work ethic is awe-inspiring. Although your frequent nights burning the midnight oil do concern me. Thank you for always encouraging me to achieve more and to dive deeper into research even though it can seem like a never-ending ocean at times. I am so grateful to have learned everything I know from you.

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ABBREVIATIONS AND DEFINITIONS

AHRs – Aryl Hydrocarbon Receptor
ATF – Bureau of Alcohol, Tobacco, Firearms and Explosives
ATSDR – Agency for Toxic Substances and Disease Registry
BAP – Benzo[a]pyrene
CDC – Centers of Disease Control
CFI – Certified Fire Investigator
 C_v – Concentration in Dose Vehicle
CYPs – Cytochrome P450
Decon – Decontamination
HHS – Health and Human Services
IAAI – International Association of Arson Investigators
IARC – International Agency for Research on Cancer
 J_{ss} – Steady-State Flux
 K_m – Distribution Coefficient
 K_p – Permeability Coefficient
 K_{ow} – Octanol/Water Partition Coefficient
NAP – Naphthalene
NFPA – National Fire Protection Association
OPP – Orthophenylphenol
PAHs – Polycyclic Aromatic Hydrocarbons
PAMPA – Parallel Artificial Membrane Permeability Assay
PASS – Personal Alert Safety System
PBI – Polybenzimidazole
PHEN – Phenanthrene
PM – Particulate Matter
PPE – Personal Protective Equipment
PTFE – Polytetrafluoroethylene
PTSD – Post Traumatic Stress Disorder
SC – Stratum Corneum
SCBA – Self-Contained Breathing Apparatus

SIR – Standardized Incidence Ratio

SMOR – Standardized Morbidity Odds Ratio

SRE – Summary Risk Estimate

SYN – SynDaver Skin

T_{lag} – Lag Time

VOCs – Volatile Organic Compounds

Chapter 1: Purpose of Research and Research Objectives

1.1. Purpose of Research

Since the events of September 11th, 2001, there has been progressively more research surrounding the toxicity, hazards, and chemical exposures for fire responders. Fire responders are a group of occupations that respond to fire emergency calls, which include firefighters, paramedics, law enforcement officers, fire investigators, and other groups. Firefighters make up the majority of the population of fire responders and are often the primary test subject for studies on chemical exposures, physiological and psychological responses, personal protective equipment (PPE) performance, resulting in numerous publications focused strictly on firefighters. Recent studies show that cancer is now the leading cause of death for firefighters overtaking heart disease and was responsible for 61% of career firefighter line-of-duty deaths between 2002 and 2017 [1].

The subpopulation of fire investigators may have an even greater risk of cancer(s) than firefighters, according to Jeff Pauley, a member of the International Association of Arson Investigators (IAAI) [2]. Both firefighters and fire investigators are frequently exposed to fireground contaminants during fire suppression, post-fire activities, fire investigation, and at the fire station. Although they frequently operate on the same fire scenes their chemical exposures are drastically different depending on when they are on the fire scene. The type of chemicals present, and their concentration levels will change over the duration of the fire and after the fire has been extinguished. However, there are a few reasons as to why fire investigators may be at equal, if not greater, risk of cancer than firefighters. In 2019, there were roughly 14,000 fire investigators in the United States, with the responsibility of inspecting fire scenes to determine the cause and ignition source [3]. This is small population compared to the 370,000 career firefighters, with an additional 745,000 volunteer firefighters [4]. Since there are significantly fewer fire investigators than firefighters, fire investigators must work more fire scenes and spend more time at each scene than the firefighters. Moreover, fire investigators have a more intimate relationship with toxic soot and microscopic particulate matter due to the nature of their job. Often duties include handling, sweeping, sifting, and digging through charred remains. These kinds of activities could unintentionally reintroduce harmful particulate matter (PM) into the air and expose fire investigators to chemical hazards.

During the summer of 2022 the International Agency for Research on Cancer (IARC) declared occupational firefighting as a class 1 carcinogen, meaning it is a known carcinogen based on “sufficient evidence”. Even if fire investigators cancer rates are higher than firefighters there is insufficient evidence as there has not been as much research on fire investigators. Whether an individual is a firefighter or fire investigator it is evident that both work in areas that are heavily contaminated and exposed to numerous toxic chemicals.

Particulate matter with a diameter of $<10\ \mu\text{m}$ is of particular concern for fire responders because it can easily penetrate the deepest parts of the respiratory tract, and the pores of human skin causing severe respiratory, heart, and skin diseases [5, 6]. When particulate matter is deposited onto the skin, the chemicals adsorbed onto the surface of these particulates may penetrate the layers of the skin and enter the blood stream of fire responders. Due to the size and abundance of PM on the fireground, avoiding contamination is nearly impossible. Lastly, post-fire exposures from handling contaminated PPE may be a large contributor to firefighter, as well as fire investigator, dermal exposures.

As a result, decontamination strategies are vital to reducing fire responder exposures. The dermal absorption exposure pathway is still not well understood for firefighters and fire investigators. Ultimately these points warrant an in-depth investigation into fire responder dermal exposures and the impact of on-scene decontamination strategies.

1.2. Research Objectives

The objective of this research is to understand the risk of dermal absorption of common fireground contaminants for firefighters during fire response either through training exercises or emergency response. An additional objective is to evaluate the effectiveness of decontamination wipes as a fireground on-scene decontamination method.

Contamination of the fire responder and their personal protective equipment (PPE) is inevitable during fire response, given that soot can be visibly seen on a person after fire response and the act of walking through the fire ground is enough to disturb and reintroduce particulate matter back into the air. Several studies have quantified toxic contaminants in air samples, in and on PPE, on the skin, and in human elimination samples, such as urine and exhaled breath samples. Although studies have quantified contaminants on the skin the extent of chemical exposure through dermal absorption is not well understood. Therefore, three different polycyclic

aromatic hydrocarbons (PAHs) will be tested for their ability to penetrate the skin under various fire response conditions such as saturated skin via sweat and increased skin temperature.

Furthermore, firefighters have begun adopting decontamination protocols into their fire response procedures. Decontamination wipes have been proposed as a simple method to remove contaminants from the skin and are becoming increasingly popular. However, there are no standards to test the efficacy of these wipes and no data on potential enhancement effects on dermal absorption caused by the decontamination wipe ingredients, if there are any. Currently there are only two studies done on decontamination wipe effectiveness against fireground contamination, both of which were conducted by wipe manufacturers. This work will investigate if there are any enhancement effects of multiple decontamination wipe products and evaluate the effectiveness of decontamination wipes by repeating previous wipe experiments while simultaneously building on their work by repeating experiments with a realistic human skin surrogate.

1.3. Limitations

1.3.1. Chapter 3: Percutaneous Absorption of Naphthalene, Phenanthrene, Benzo[a]pyrene, and Orthophenylphenol in the Porcine Skin Model

The *in vitro* flow-through diffusion cell experiment is a valuable tool for initial screening, comparative studies, and mechanistic insights into permeation processes of drug formulations, chemical penetrants, and absorption enhancers. Although large amounts of data can be collected from a relatively short and efficient *in vitro* flow through experiment there are some limitations. *In vitro* diffusion cell experiments use excised animal/human tissue or synthetic membranes which cannot fully replicate the complexity of *in vivo* conditions, where factors like blood circulation, metabolic activity, and cell interactions play a significant role. The stratum corneum properties between animal models can vary drastically, making comparisons between different animal models challenging. Additionally, anatomical differences can change the properties of the stratum corneum and absorption results. Generally, the process of absorption is complex and can involve multiple mechanisms, which may be oversimplified *in vitro*.

1.3.2. Chapter 4: Impact of the Fireground Environment on the Percutaneous Absorption of Polycyclic Aromatic Hydrocarbons

The previously mentioned limitations of the *in vitro* flow-through diffusion cell experiment also apply to this chapter. Further limitations of this experiment include the

environmental conditions tested in this study might not perfectly mimic the change in absorption behavior of the skin because changes in skin and body temperature on the fire ground is a dynamic process. Humidity variations are also factors that can affect skin permeability and these factors were not considered during this experiment.

During the wipe ingredient experiments the nature of the exposure and addition of decontamination wipe ingredients resulted in prolonged contact with the skin over several hours. This is unlikely to occur as firefighters would return to the fire station, bathe, and change clothes after leaving the fire scene.

1.3.3. Chapter 5: Chemical Absorption Comparison of a Synthetic Skin Model to Porcine Skin

The previously mentioned limitations of *in vitro* flow-through diffusion cell experiment also apply to this chapter.

1.3.4. Chapter 6: Decontamination Wipe Efficacy Trials on Various Surfaces

The liquid contaminants used in previous wipe manufacturer and this study do not represent realistic chemical exposures experienced on the fireground. The wipe efficacy reported in previous wipe studies and this one may be different for vapor and particulate contaminants.

Chapter 2: Literature Review

2.1. The Fireground

The fireground is one of the most dynamic and dangerous work environments. Each fireground is unique and will vary in size, location, fuel source, and contamination area. The limits of the fireground are defined by the incident commander. For this literature review, the fireground will be defined as the structure and materials burned in an area where a fire occurred, the area contaminated by the fire, and the closely adjacent areas occupied by emergency responders.

Each year, numerous victims and fire responders are injured and killed during fire response [7]. The unpredictable nature of each fire provides several challenges for even the most tactically minded, seasoned firefighter. Fires themselves are unique and their behavior will vary based on several factors such as the fuel source, nature of the fire, environmental conditions, location of the fire, and available oxygen. Additionally, changes in building layouts, construction materials, and furnishings found in the average home/building have changed fire dynamics and fire behavior [8]. Furthermore, adoption of man-made and polymer-based products over traditional and natural products in structures result in fires burning quicker, hotter, and with more toxic chemicals and increased particulate matter generated that all negatively impact fire responder health [9].

2.2. Changes in the Fireground

2.2.1. History of Human Structures

Advancements in construction materials, tool technology, agriculture, and architecture have allowed humans to move from the nomadic lifestyles to settling down and living in a single area for extended periods of time in permanent shelters. Advanced tools allowed for rock-cut architecture (structures created from existing rocks/stones) used by the ancient Babylonians. The invention of combining organic material like mud, sand, clay, and water allowed for people to create a consistent and repeatable building material that could be used to assemble a structure. Subsequently mud bricks, terracotta, and adobe quickly became popular building materials for ancient civilizations like Ancient Egypt. The use of brick-like building materials continued for thousands of years and is still used in some parts of the world today. Large stonework dominated advanced architecture for hundreds of years demonstrated by the Parthenon in Ancient Greece, castles in Medieval England, and Tempietto di San Pietro in modern Europe. Table 1 shows the

historic progression of human structures starting with prehistoric structures such as the Inuit's Tupiq, pit-houses, and huts progressing to modern buildings such as the new Hunt Library found on NC State University's Centennial Campus.

The First Industrial Revolution (1760 – 1840) and Second Industrial Revolution (1870 – 1920) were periods of rapid advancements which gave rise to modern construction techniques and architecture. During these periods, advancements in construction materials such as mass-produced iron, steel, and glass allowed for larger sized projects. Buildings could now be constructed much taller than ever before, illustrated by the Flatiron Building in New York City in Table 1, allowing for densely populated cities. Balloon framing and light wood frame construction replaced traditional timber frame construction and allowed for domestic housing to boom [10]. This led to people expanding outward from the overcrowded cities, creating the suburbs we are familiar with today. With the explosion of housing in the United States so did the risk of structural fires. The number of house fires has been consistent ranging from 350,000+ to 380,000+ over the past decade (2010-2019). However, the number of residential building fire injuries has decreased steadily from 2011 until 2017 where the trend reversed and the number of injuries has been rapidly increasing, suggesting a change in the home or fire response [11].

Table 1: Images of human shelters and structures throughout history

 <p>Inuit Tupiq 9000 – 5000 BC</p>	 <p>Mammoth bone structure 9000 – 5000 BC</p>	 <p>Brick Structure of Babylon 1770 -1670 BC</p>
 <p>Ancient Egypt Pyramid 3150 – 300 BC</p>	 <p>Parthenon, Ancient Greece 600BC</p>	 <p>Bodian Castle, England, 1400s</p>
 <p>Tempietto di San Pietro, Europe, 1502</p>	 <p>Flatiron Building, New York City, 1903</p>	 <p>James B. Hunt Jr. Library, North Carolina, 2013</p>

2.2.2. Legacy vs Modern Homes

After continued advancements in construction techniques, material technology, furnishings, and consumer preferences, the average American household material composition continues to evolve, resulting in everchanging fire dynamics and fire behavior. Homes are commonly classified as either a Legacy or Modern home based on the year it was built and the materials used in construction and furnishings. Legacy homes are considered to be homes from the 1950s or earlier and furnished with natural materials, for example cotton-based furnishings and curtains. Whereas modern homes are what most people live in today and have substituted the traditional materials found in legacy homes with cheaper, mass produced, synthetic materials such as gypsum board, engineered flooring and joists, polyester furnishings, and electronic materials, seen in Table 2. The differences in construction material, floor plans, furnishing materials, etc. between legacy and modern homes have a large impact on the fire dynamics [12].

Table 2: Differences in Construction Materials used in Legacy and Modern Homes adapted from Kerber (2012) [12]

<u>Construction Material</u>	<u>Legacy</u>	<u>Modern</u>
Wall Linings	Plaster and Lath	Gypsum Board
Structural Components	Old Growth Lumber	New Growth Lumber, Wood Trusses, and Engineered I-Joists
Windows	Single Glazed (Wood Framed)	Double Glazed (Vinyl Framed)
Interior Doors	Solid Core	Hollow Core, Composite Hollow Core

2.2.3. Effects of the Modern Household on Fire Dynamics

Fires are consistently responsible for \$6 – \$10 billion dollars in damages to American property every year since 1980 [13]. Sadly, fires continue to kill over 2,500 civilians and over 60 firefighters annually [7]. The rate for firefighter deaths occurring outside structures or from cardiac arrest has declined, meanwhile, firefighter deaths occurring inside structures has increased over the past 30 years. The changes in these trends illustrate that firefighters struggle to navigate the fireground safely.

Changes in home size, adoption of open floor plans, furnishing materials, and construction materials all play significant roles in fire behavior. Based on United States Census data, homes have increased in average area from 144 m² in 1973 to over 232.3 m² in 2008 [12]. The increase in living space commonly comes from homes being built with multiple stories. The number of two-story homes increased from 23% of homes in 1973 to 56% in 2008, whereas the percentage of single-story homes decreased from 67% to 44% in the same period, shown in Figure 1. If a fire ignites on the first floor of a multistory building, then the floors above create a smoke layer that remains above the fire and allows the fire to grow. The fire will eventually become ventilation limited as the fuel from the first floor is consumed. At this point a large introduction of air has the potential to increase flashover conditions.

Social trends are important for the housing market as buyers seek to have the latest and greatest things. One recent trend is open floor plans. Modern homes use features such as open floor plans, taller ceilings, two-story foyers, and great rooms to highlight a luxurious style of living and entice buyers. Ceiling heights are now 1.8 – 2.5 times higher than in traditional homes [12]. Open floor plans are removing walls to create longer sightlines within homes. The increased volume due to higher ceilings and larger room sizes ultimately require more water and resources to extinguish a fire. This makes fires more difficult to contain because of the lack of compartmentation. The simple, yet effective, tactic of closing a door to confine a fire is no longer a possibility in newer home floor plans. These trend-forward modern features remove compartmentation, add volume, and contribute to rapid smoke and fire spread.

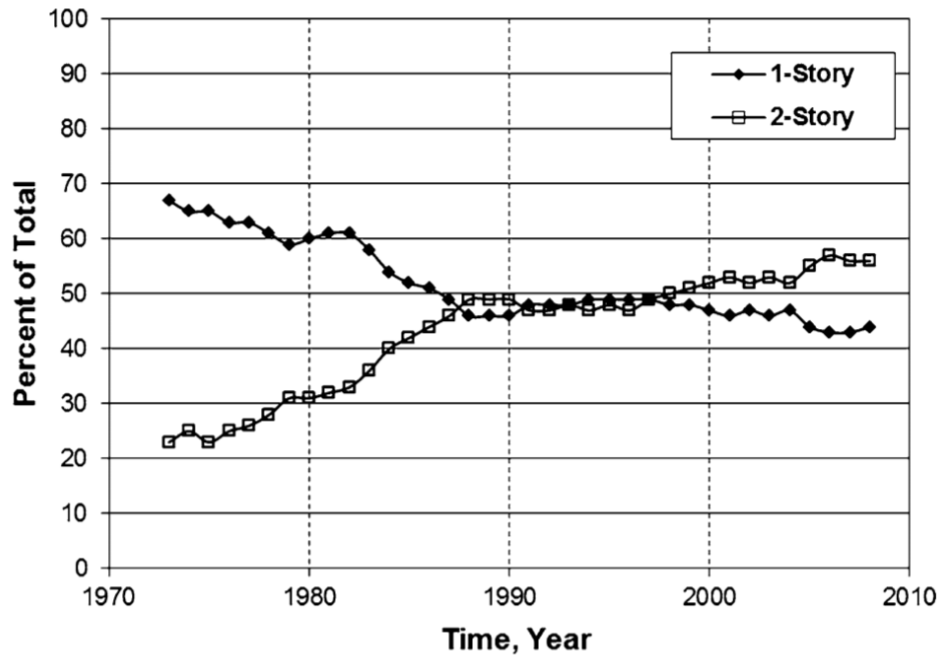
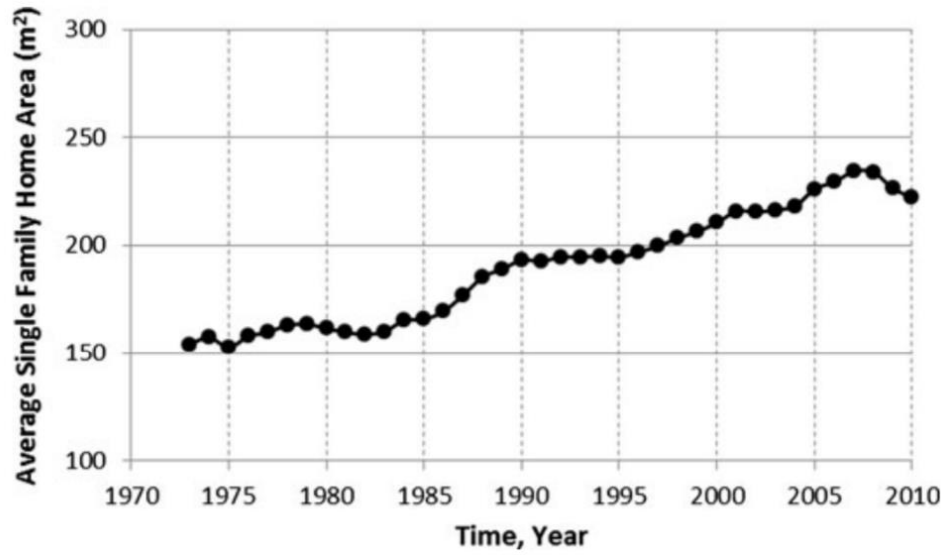


Figure 1: (Top) Average square footage (m²) of new single-family homes from 1973 – 2010
 (Bottom) Percentage of single family homes as 1-story or 2-story construction from 1973 – 2008 [12]

The widespread adoption of plastic and synthetic materials in the modern world has also significantly impacted the type of materials used in home construction and products inside the average household. In 2015, the United States alone consumed over 300 million tons of plastic products [14]. The adoption of plastic and polymer-based products has created a new challenge of rapid fire spread for firefighters. Synthetic materials and natural materials have similar total heat release; however, synthetic materials burn hotter and quicker, meaning they release the same amount of heat and energy in a shorter amount of time. For firefighters this means they have significantly less time, approximately 10 times less, to combat the fire before the scene reaches flashover conditions [8, 12, 15, 16]. Figure 2 illustrates this difference in time to flashover by igniting identical rooms filled with legacy and modern furnishings.

Numerous studies have established that the smoke produced from structural fires contains a multitude of toxic compounds [17, 18, 19, 20]. For a fire, the contents of the fuel sources can define the behavior and dynamics of the fire, but also the toxicants produced to which fire responders will be exposed to. Common household items such as appliances, paints, and cleaning products pose serious hazards upon combustion to the health of the fire responders. Given the extensive range of applications for the materials subjected to combustion, it is reasonable to assume that every structural fire will emit smoke with high concentrations of toxic compounds. The types of chemical hazards produced during a typical fire can be found in Table 3.



Figure 2: Images from a time-lapse demonstrating the time to reach flashover conditions of a room filled with legacy vs modern room furnishings [16]

2.3. Hazards of the Fireground

The fireground is a dangerous ever-changing scene as the fire progresses through its life. Once fire responders arrive on scene, they will encounter several types of hazards. The most obvious hazard is the fire, accompanied by the intense temperatures and radiant heat perpetuated by the burning fuel sources. However, researchers and scientists are becoming increasingly concerned about the chemicals and combustion products created as a result of burning synthetic and electronic materials. Due to the presence of toxic combustion products, responders are beginning to exercise greater precaution for routine structure fires, employing tactics commonly used in responses to hazmat (hazardous materials) scenarios.

2.3.1. Thermal Hazards

Fires have five stages: incipient, growth, flashover, fully developed and decay, illustrated in Figure 3. The incipient stage is where the fire progression is limited to a single fuel source and the heat produced is unable to transfer to adjacent fuel sources. During the growth stage the rate of heat released from the fire increases to the point where the heat transferred from the fire and the combustion products begin pyrolyzing adjacent fuel sources. As the fire progresses towards the fully developed stage, flashover is likely to occur. Flashover is a transitional phase in the development of a compartment fire in which surfaces exposed to thermal radiation reach its ignition temperature more or less simultaneously and fire spreads rapidly throughout the space resulting in full room involvement or total involvement of the compartment or enclosed area, defined by National Fire Protection Agency (NFPA) 921 [21].

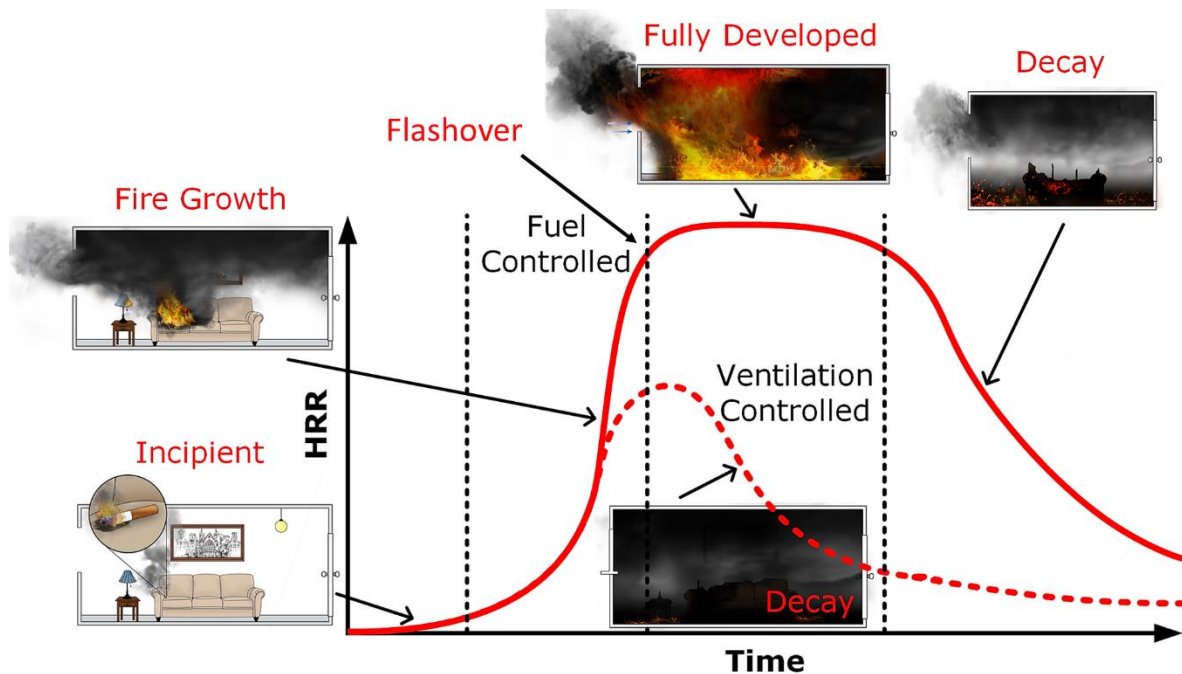


Figure 3: Illustration of the stages of fire development (HRR = Heat Release Rate) [22]

Fires have three ways of transferring heat: conduction, convection, and radiation. Conduction is where heat is transferred within solids or between contacting solids, convection is the movement of heat through liquids or gases, and radiation is the transfer of heat by electromagnetic waves [22]. Radiation is the method of heat transfer firefighters are most concerned about and is described as the amount of heat transmitted to a specific area of clothing in calories (the amount of heat required to raise a gram of water by one degree Celsius). Ordinary fireground conditions can range in temperature from 140 – 570°F and 0.05 – 0.6 cal/cm²/s. In the worst conditions, typically seen during flashover, temperatures can exceed 1,000°F and radiation levels can exceed 2.0 cal/cm²/s. The protective turnout ensemble worn by firefighters is designed specifically to protect against radiant heat. Performance specifications require firefighter turnout gear to provide several minutes of protection under ordinary fireground conditions.

Firefighters are extremely mindful of the potential for a flashover due to the fast-changing and extreme conditions associated with it, including temperatures exceeding 1,000°F in a matter of seconds. Firefighters, even when wearing all the recommended turnout gear, are not likely to survive in a compartment that undergoes flashover [8, 22]. After flashover, the fire matures and is now fully developed. During this point the fire reaches peak heat release. The last

stage of a fire is when the fuel sources begin to deplete and heat output decreases, the intensity and threat of the fire declines, ultimately becoming extinguished. The extinguished fire scene is then classified based on time into one of four categories: 1) hot scene A where the fire has been extinguished but overhauls has not yet commenced, 2) hot scene B where the fire has been fully extinguished/overhauled for less than two hours, 3) warm scene where the fire has been fully extinguished at least two hours but less than 72 hours, and 4) cold scene where the fire has been fully extinguished for at least 72 hours and not generating detectable or visible dust, fumes, mists, particulates, gases, vapors or aerosols [23].

2.3.2. Chemical Hazards

The chemical hazards of a fireground have long been a secondary concern as thermal hazards present an immediate threat for firefighters. However, as firefighter's turnout gear has improved significantly against thermal hazards the same cannot be said about the protection against chemical hazards, which are now a primary concern for the fire service industry. The number and severity of chemical hazards has increased as more polymer-based products, plastics, electronics, cleaning products, paints, etc. are used in American households and subsequently burned in house fires. When these products burn, they create toxic byproducts which can have serious acute and chronic health effects for firefighters.

Gasses and vapors are frequently encountered chemical hazards on the fireground. These contaminants have been found in the air during fire-suppression activities and during post-fire activities, as well as in the breath of firefighters who were involved in fire suppression [19, 20, 24]. The concentration of these contaminants decreases over time but can remain at the fire scene for several hours after the fire has been extinguished. Due to this extended potential for exposure, it has been recommended that firefighters continue to wear their self-contained breathing apparatus (SCBA) during overhaul [24]. Table 3 lists some toxic compounds that have been observed over permissible exposure limits in fireground environments and attributes their presence to the combustion of specific materials frequently found in common structures.

Particulate matter (PM) is the microscopic solids mixed with gas and liquid droplets, sometimes even acids, organic chemicals, metals, or dust particles, that are small enough to remain suspended in air, and are the main components of soot and smoke. The size of the individual particles can be divided into two classes, both important to understanding inhalation exposures and adverse health effects. Particles 10 micrometers in diameter (PM₁₀) can be inhaled

into the lungs and reach the bloodstream, causing severe health effects. Finer particles, less than 2.5 micrometers in diameters (PM_{2.5}), can pose even greater health risks because they can penetrate deeper into the respiratory system [25]. Particulate matter is a serious issue alone but is then compounded when factoring the adsorption of toxic chemicals onto the particle surface. Upon exiting a fireground environment, it is nearly impossible to remain unexposed to the particulate matter present at the scene.

Table 3: Toxic Combustion By-products of Common Materials in a Structural Fire

Combustion By-product	Responsible Materials	Common Applications	Toxic Health Effects
Ammonia [26]	Polyurethane foams Treated woods	Mattresses Hardwood flooring	Respiratory irritation, cardiac arrest, death
Carbon Monoxide [27]	Most natural and synthetic polymers	Building construction materials	Headache, nausea, vomiting, cardiac arrest, respiratory arrest, pulmonary edema, seizures, death
Hydrogen Cyanide [28]	Nylon Polyurethane Acrylonitrile	Insulation Carpets Appliances	Headache, nausea, vomiting, skin and eye irritation, abnormal heartbeat, death
Hydrogen Sulfide [29]	Cotton Wool Asphalt	Clothing Furniture Roofing	Respiratory distress, cardiac distress, hypotension, death
Nitrogen Dioxide [30]	Wood Nylon Acrylonitrile butadiene styrene	Upholstery Fiberglass	Chemical burns, respiratory irritation, accumulation of fluid in lungs, death
Sulfur Dioxide [31]	Wood Copper Lead	Electrical wiring Electronic devices	Respiratory damage, nausea, vomiting, death
Polycyclic Aromatic Hydrocarbons [32]	Polytetrafluoroethylene (PTFE) Resins Rubbers	Paints Varnishes Cleaning supplies	Cancer, birth defects
Phthalate Esters [33]	Poly(vinyl) chloride Plasticizers Clay derivatives	Piping Furniture Toys	Digestive irritation, death

2.3.3. Physiological and Physiological Hazards

The extreme conditions of a fire can push a firefighters body to its limits and evoke serious physiological responses. Furthermore, traumatic experiences can have a long-lasting effect on a firefighters mental health.

The average weight of the full firefighter ensemble (turnout gear + SCBA) weighs on average 26.2 ± 1.8 kg. The added stress placed on the body by wearing the protective ensemble can increase firefighter's heart rate to 67 – 83% of their max heart rate without exposure to the extreme temperatures experienced during live-fire scenarios [34, 35, 36]. When the extreme temperature of a fire is introduced the body's physiological responses are extensively challenged. During firefighting activities the heart accelerates, increasing aortic blood flow, peak velocity, stroke volume, and increases to age-predicted maximal values [34, 37, 38, 39, 40, 41]. As the heart works tirelessly, the body begins to sweat in an attempt to cool the body through evaporative cooling [42, 43, 44]. However, regardless of the environmental conditions encountered, evaporative cooling will reach a maximum value, putting the body at risk of overheating in these environments [36, 43]. With insufficient methods of cooling the body, core and skin temperatures begin to rise and have been shown to reach $35 - 40^{\circ}\text{C}$ [34, 35, 36, 37, 38, 39, 40, 41]. An elevated core temperature and increased heart rates are natural physiological responses of increased physical activity, however if elevated for an extended period it can result in fatal injuries. Stress or overexertion was the leading cause of fatal injury for firefighters in 2019, accounting for 36 of the total 62 on-duty firefighter fatalities [7].

Firefighters also undergo acute and chronic psychological responses from their occupational hazards. Studies have repeatedly shown that firefighters are more conscientious of their body and performance while wearing their protective ensemble during simulated firefighting activities and/or in hot environments [35, 36]. Common psychological responses including thermal sensation, physical exertion, respiratory distress, anxiety, tiredness/energy level have all been shown to be increased during firefighting activities [34, 35, 40]. The strenuous requirements of firefighting can impair cognitive function and cause more mistakes even when conductive simple cognitive tasks [35]. It is evident that firefighter's senses are heightened during firefighter activities, however these psychological responses are quickly relieved once the firefighter is removed from the scene.

Firefighters have high rates of exposure to potentially traumatic events (PTE). These traumatic events often meet the Diagnostic and Statistical Manual of Mental Disorders Criteria A for Post-Traumatic Stress Disorder (PTSD) [45]. Examples of these PTEs include catastrophic injury to self, coworkers, victims, rendering aid to seriously injured or vulnerable victims, and exposure to death and dying. Rates for PTSD have been reported as high as 18 – 37%, approximately 2 – 4 times higher than the general public, however with more rigorous diagnostic procedures (e.g., verification of Criterion A and functional impairment rather than symptom cutoff alone) rates of PTSD decreased to 5 – 13% among firefighters, which is comparable to the general public [45]. However, more data is needed before a definitive conclusion on firefighter's increased risk of PTSD can be made. PTSD is not the only chronic psychological responses firefighters are at risk for, sleep disturbances are relatively common among firefighters, with one study finding a rate of 51.2% of the study population [46]. Sleep disturbances increase the risk for general psychological distress, psychosomatic alteration, suicidal ideation, and unhealthy alcohol and drug use. Despite this, time on the job was found to be a protective factor, suggesting that people develop different coping mechanisms [46].

2.4. Fire Responders

2.4.1. Firefighters vs Fire Investigators

Firefighters, police officers, and emergency medical technicians are the most common fire responders, however, paramedics, detectives, sheriffs, state troopers, rescue personnel, fire investigators, and hazardous material workers may also be present at the fire scene. Firefighters and fire investigators are two unique groups that provide distinct functions and will be the main focus in this literature review. Firefighters are responsible for victim rescue, preventing the spread of the fire, preservation of property, and extinguishing the fire if possible. Their responsibilities require them to operate near the fire when it is most dangerous. Fire investigators only begin working once the fire has been extinguished. Their primary responsibility is to investigate the fireground to determine the cause or source of the fire, identify any abnormal materials like accelerants, and collect evidence. Both firefighters and fire investigators spend a significant amount of time on the fire scene. Due to their prolonged and repeated exposures, firefighters and fire investigators have the greatest risk out of all fire responders for exposure to carcinogenic fireground contaminants.

2.4.2. Fire Responder Exposures

The nature of firefighter and fire investigator exposures are different simply because they work on the fire ground at different stages of the fire. Firefighters work while the fire is raging and the majority of fireground contaminants are produced. While the fire is progressing through its life stages the burning fuel sources are producing gases, vapors, particulates, smoke, soot through various combustion reactions. During the apex of the fire, gases and vapors are present in the highest concentration. Firefighters also walk through the burning structures frequently and navigate through the smoke that has been trapped. The particulate matter of the smoke is deposited on the surface of the gear and on the skin of firefighters [47, 48, 49].

Meanwhile, fire investigators only begin to work once the fire has been extinguished and may not even arrive on the scene until several days have passed. As more time passes after the fire has been extinguished the concentration of volatile compounds decrease as they off-gas [50, 51]. However, fire investigators are more susceptible to particulate matter and soot exposure. Actions such as walking through the scene, collecting evidence, sifting through burnt material and ash disturb the particulate matter and can reintroduce it to the environment.

Working in environments with several sources of contaminants and working near said sources almost guarantees that any clothing or PPE worn will be contaminated. Polycyclic aromatic hydrocarbons are a common contaminant found at nearly every fireground. They have been repeatedly found on the skin, urine, exhaled breath, and turnout gear of firefighters [24, 47, 48, 52, 53]. Other contaminants such as flame retardants, plasticizers, dioxins, and furans have been found on firefighter turnout gear [20, 54, 55]. In the air, toxic compounds such as VOCs, aldehydes, acrolein, carbon monoxide, benzene, nitrogen dioxide, sulfur dioxide have been found [19, 24]. Fire investigator chemical exposures are substantially unstudied when compared to the numerous studies conducted on firefighters and their chemical exposures.

2.4.2.1. Exposure Pathways

There are three main exposure routes in which fire responders can be exposed to chemicals are inhalation, dermal, and ingestion, although the ingestion route is often neglected because exposure is assumed to be negligible relative to fire response exposures. Inhalation is the primary exposure pathway of concern for combustion products for fire responders because of the lungs sensitivity and several fireground contaminants with respiratory effects. However, this pathway can be significantly mitigated if an SCBA is worn properly, as shown in Figure 5. For

firefighters, a fit test is conducted to ensure a tight seal between the facemask and the face to prevent any environmental air, particulates, or gases from entering. Unlike firefighters, fire investigators are not required nor incentivized by the NFPA to wear an SCBA meaning they are at greater risk to exposure to chemicals off-gassing from the fire scene. The second exposure pathway is dermal absorption. This is the most difficult exposure pathway to assess because of the variability between individuals and the difficulties in sampling contaminants from the skin. The role a firefighter has, whether it be attack, search and rescue, ventilation, or hose operator, can also influence their chemical exposure and skin contamination. Firefighters who enter a structure and use their hands to move and clear debris will have higher amounts of contaminants on their gear and skin than those who are outside the structure, such as the engine operator [47]. The same can be assumed for fire investigators, although no research has been conducted on fire investigators dermal exposure to fireground contaminants.

2.4.3. Current Fire Responder Personal Protection Equipment

As previously discussed, the fireground is filled with several types of hazards and to protect themselves both firefighters and fire investigators wear PPE to mitigate their risks and exposures to these hazards. The modern firefighter ensemble is vastly different to the garments worn by the earliest firefighters. Modern firefighters have several layers of protection from the hazards they encounter during a fire. The turnout ensemble is constructed of three layers: an outer shell, with the outer shell on top facing the environment, a thermal liner closest to the skin, and a moisture barrier sandwiched between these two layers, depicted in Figure 4. Each layer of the turnout ensemble has a specific function; the thermal liner provides insulation and thermal protection, the moisture barrier prevents moisture from penetrating the ensemble thus preventing burns, and the outer shell protects against cuts, abrasions, and liquids. The outer shell is commonly made from polybenzimidazole (PBI), meta-aramid, and para-aramid fibers in unique combinations and constructions to impart specific thermal and heat resistance. The moisture barrier contains either a woven or nonwoven fabric with a polytetrafluoroethylene (PTFE) membrane film laminated onto the fabric. The thermal liner itself has two layers, the face cloth, which is closest to the skin and a batting, closest to the moisture barrier.

To ensure firefighters are protected, the turnout gear and clothing must pass performance requirements set by the National Fire Protection Association (NFPA). Examples of some performance requirements include, the protective garment elements shall have an average

Thermal Protective Performance rating of 35.0 or greater, no liquid shall penetrate the garment, garment composite shall have a Total Heat Loss of no less than 205 W/m², garment outer shell have a Radiant Protection for at least 20 seconds. Further performance criteria for modern turnout gear can be found in *NPFA 1971 – Standard on Protective Ensembles for Structural Fire Fighting and Proximity Fire Fighting* [56].

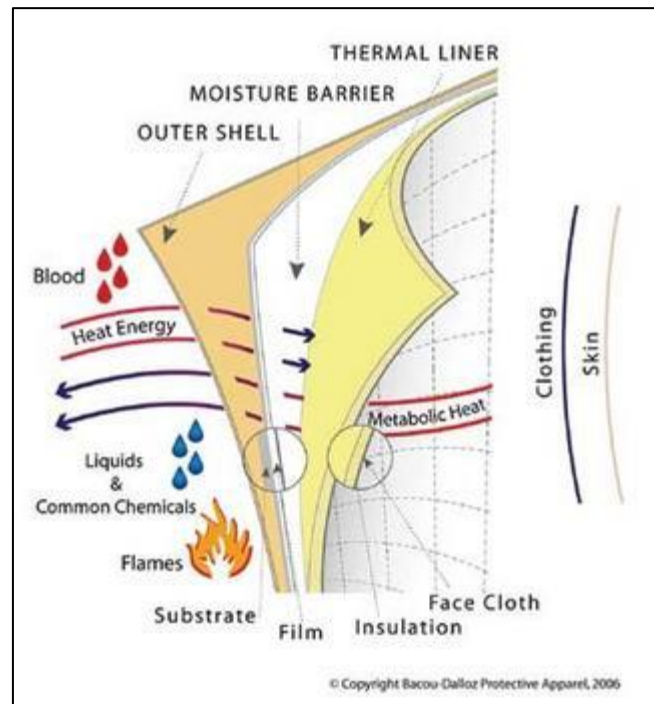


Figure 4: Diagram of the layers in turnout gear coats and pants [57]

In addition to the layered turnout coat and trousers the modern firefighter protective ensembles include a helmet, face mask, boots, gloves, a self-contained breathing apparatus (SCBA), and a personal alert safety system (PASS) device, seen in Figure 5. The particulate-blocking protective hood has been the most recent addition to the firefighting turnout ensemble. It was introduced in late 2015 in response to a study by the International Association of Firefighters discovered that firefighter ensembles are susceptible to particulate penetration at interface areas.



Figure 5: Diagram of Firefighter Turnout Gear [58]

Unlike firefighters, fire investigators do not require the same level of thermal protection since they work on the fireground after the fire has been extinguished. This greatly impacts the requirements of PPE for fire investigators. The degree of thermal protection is directly related to the time that has transpired since the fire was extinguished. Hot scenes may require firefighter turnout gear. In a warm scene fire investigators may swap the turnout gear for coveralls. At cold scenes where little to not thermal protection is required; some investigators will elect to wear more comfortable clothing and conduct their work in long pants and long sleeve t-shirt. Figure 6 shows the different levels of PPE worn by fire investigators according to the time-based scene classification system. A half-mask respirator is recommended, but not required, to be worn in Hot/Warm scene. The decision to wear respiratory protection is governed by the comfort of the individual. Currently there are no standards or requirements established for fire investigator PPE. The International Association of Arson Investigators (IAAI) is working on establishing these standards. In 2020 the IAAI released the Fire Investigator Health and Safety Best Practices document, a white paper that describes the health hazards on firegrounds, health and safety best practices, PPE guidelines and protection categories [23].

Figure 6: Images of Fire Investigator PPE worn on fire grounds based on time-based characterization of the scene

Hot Scene



Warm Scene



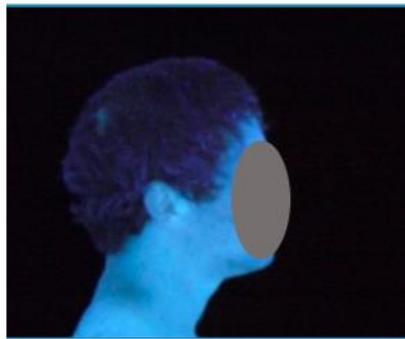
Cold Scene



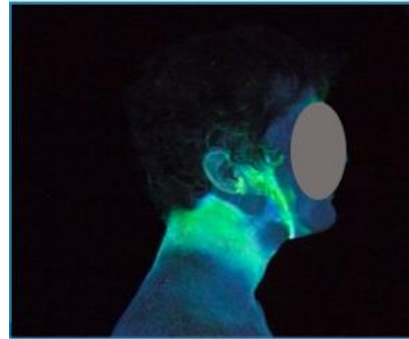
2.4.4. Gaps in Fire Responder PPE Protection

Although the firefighter turnout ensemble provides excellent protection against thermal hazards, it lacks sufficient chemical and particulate protection. In 2015, the International Association of Firefighters commissioned experiments to evaluate particle penetration of firefighter ensembles. Full turnout gear worn in conjunction with a SCBA was worn by a test subject and placed in a chamber filled with particulates. The test subjects were exposed to high-level concentrations of silica powder particles tagged with fluorescent tracers having particle sizes ranging from 0.1 – 10 μm [49]. Upon photographic analysis, depicted in Figure 7, a significant amount of particle contamination was visible around the neck, wrist, thigh, and calf areas. These contaminated areas of the body correspond to interface areas between the different pieces of the turnout ensemble. Figure 7 picture B, displays a clear line where the SCBA would sit while being worn. The face has little to no particle contamination which reinforces the protection an SCBA provides while being worn, which indicates that dermal exposure is the most popular pathway for combustion products and other fire scene contaminants. This study was one of the first to illustrate the desperate need for increased chemical and particulate protection for firefighter turnout gear. Subsequently, the traditional hoods were redesigned to implement a particulate-blocking layer.

Fire investigators on the other hand do not have a standard uniform. Each type of protective garment worn by fire investigators would need to undergo chemical liquid, vapor, and/or particulate penetration tests, similar to firefighter turnout gear to understand the amount of protection for fire investigators. It has already been shown that firefighter turnout gear is susceptible to particulate penetration. Long sleeved shirts and pants would be expected to provide little to no protection against particulates due to the large interface openings and openings in the garments themselves. Tyvek® coveralls, although untested, may provide adequate chemical protection as some Tyvek® products have sealed seams and are cuffed at the wrists and ankles which could minimize particulate penetration. Ultimately, the gaps in PPE testing, standardization, and performance criteria leave fire investigators uninformed about their exposures to the chemical hazards present at firegrounds.



(A)



(B)



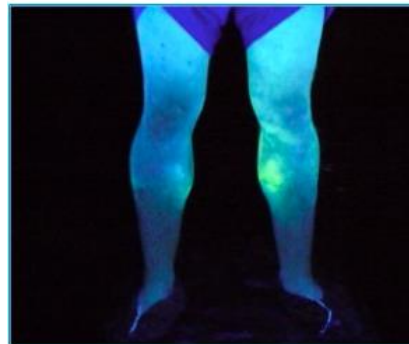
(C)



(D)



(E)



(F)

Figure 7: Fluorescent particle deposition on the skin after fluorescent particle exposure while wearing full turnout gear. Part A and B show the before and after of the head area. Part C and D show the before and after of the torso area. Part E and F show the before and after of the lower body area [49].

2.4.5. Health Studies on Firefighters

There have been several health studies on firefighters in response to thermal hazards, such as determining physiological responses in elevated temperature environments. However, health studies in response to chemical hazards are more difficult to conduct. These studies require a large sample size, detailed exposure documentation, and can continue for years sometimes across decades. Despite these challenges there are several studies that have investigated cancer incidence and risk in firefighters. American studies have examined cancer incidence rates of firefighters in California, Florida, Illinois, Massachusetts, Philadelphia, and Washington dating back to 2005 [59, 60, 61, 62, 63].

Individual studies have found increased risks for diseases: melanoma, multiple myeloma, acute myeloid leukemia, Hodgkin's lymphoma, and cancers: prostate, colon, brain, bladder, kidney; as well as increased incidence of thyroid, bladder, testicular, cervical cancers and Hodgkin disease [59, 60, 61, 62, 63]. As more individual state and regional studies were conducted larger meta-analysis studies could be conducted to find more definitive trends across the occupation. In 2006 a meta-analysis of 32 studies sought to determine firefighters' cancer risk quantitatively and qualitatively. Twenty-one cancers were assessed to be "not likely," "possible," or "probable" given a three criteria assessment: "pattern of meta-relative risk association", "study type", and "consistency". The results indicated that firefighters had a probable cancer risk for multiple myeloma, non-Hodgkin lymphoma, and prostate cancer, while testicular cancer was evaluated to be probable after having the highest summary risk estimate. Additional cancers that were evaluated to be "possible," included buccal, stomach, colon, rectum, skin, testicular, brain cancer, malignant melanoma, and leukemia [64].

One of the largest studies on cancer incidence in firefighters to date was done in 2014 and included nearly 30,000 career firefighters from San Francisco, Chicago, and Philadelphia from 1950 through 2009 (59 years). The study population included individuals who were of any race and employed for at least one day in fire departments in San Francisco, Chicago, or Philadelphia from 1950 to 2009. All cancer incidence was slightly above expectation. Cancers with significant excess included esophagus, large intestine, kidney, and lung cancer and additional excess included buccal, laryngeal, and pharynx cancers and malignant mesothelioma [61].

In 2010 the IARC released a report that examined all health studies investigating cancer incidence in firefighters. This report found three types of cancer to show significant summary

risk estimates. Incidence of testicular cancer was roughly 50% in excess based on six studies and about 150 cases. Incidence of prostate cancer was about 30% in excess based on 17 studies and approximately 1800 cases. Lastly, incidence of non-Hodgkin lymphoma was 20% excess based on several studies and more than 300 cases [65]. Overall, this report declared that firefighting to be likely carcinogenic. The abundant amount of data has persuaded the U.S. government to recognize the inherent risks that are now associated with firefighting. A new law, the Firefighter Cancer Registry Act of 2018, requires the Centers of Disease Control (CDC) to maintain a database of the firefighters who get cancer [66].

The previously mentioned studies have found several connections, of varying degrees, between firefighting and an increased risk of various of cancers and diseases, found in Table 4. However, even though multiple studies have found correlations between firefighting and cancer the findings may underestimate the risk of cancer in the fire service industry. Multiple studies used cancer registries or databases to identify their study population [59, 60, 62, 63]. One issue when using registries or databases to identify a study population is an under or over estimation of the number of people to include in the study. Individuals may go untested, misdiagnosed, or miscategorized, which may lower or inflate the total number, which in these studies influences the number of cancer cases.

Additionally, nearly all studies compared firefighters' cancer incidence to that of the general public [59, 60, 61, 62, 63]. Now generally, firefighters are healthy individuals because of their training and the physical requirements of the job. Health comparisons between firefighters and the general public can be skewed based on the healthy worker effect. The healthy worker effect may reduce the death rate among workers by 70 – 80% relative to the general population. The magnitude of this effect may be even larger in firefighters because of the rigorous fitness demands of the profession. Despite this fact, firefighters are found to have increased incidence of cancer than the general public, which may speak to the severity of the chemical exposure experienced during their work.

Table 4: Summary of previous firefighter health studies

Study	Location	Length of Study	Study Population	Measurement Parameter	Results of the Study
Risk of Cancer Among Firefighters in California 1988 – 2007 [59]	California	1988 – 2007	4000 male firefighters	Odds Ratio	Significantly elevated melanoma, prostate, and brain cancer for all firefighters. Three cancers were significantly elevated among all firefighters and white firefighters: esophagus, lung cancers, and acute myeloid leukemia. Three cancers were significantly elevated among all firefighters combined and firefighters of other race/ethnicity: kidney cancer, multiple myeloma, and overall leukemia.
Cancer Incidence in Florida Professional Firefighters, 1981 to 1999 [60]	Florida	1981 – 1999	35000 male and 2000 female firefighters	(SIR) Standardized Incidence Ratio	970 male and 52 female cases of cancer were identified. Male firefighters had significantly increased risk of bladder (SIR=1.29), testicular (SIR=1.60), and thyroid cancers (SIR=1.77). Female firefighters had significantly increased risk of overall cancers (SIR=1.63), cervical cancer (SIR=5.24), and Thyroid cancer (SIR=3.97) and Hodgkin disease (SIR=6.25).
Mortality and cancer incidence in a pooled cohort of firefighters from San Francisco, Chicago and Philadelphia (1950 – 2009) [61]	Philadelphia, Chicago, and California	1950 – 2009	30000 male firefighters	(SMR) Standardized Mortality Ratio and (SIR) Standardized Incidence Ratio	Excess cancer mortality and incidence for digestive (SMR=1.26, SIR=1.17), respiratory (SMR=1.10, SIR=1.16) cancers, malignant mesothelioma (SMR=2.00, SIR=1.16). However, evidence of excess lymphatic or haemopoietic cancers were lacking.
Cancer incidence among firefighters in Seattle and Tacoma, Washington (United States) [67]	Seattle and Tacoma, Washington	1974 – 1989	2500 male firefighters	(SIR) Standardized Incidence Ratio	Elevated risk of prostate cancer compared to general population (SIR=1.4). Slightly elevated risk of colon cancer compared to general population (SIR=1.1). The risk of colon cancer increased with duration of employment.

Table 4 (continued)

Cancer Incidence Among Male Massachusetts Firefighters, 1987 – 2003 [63]	Massachusetts	1986 – 2003	2200 white male firefighters	(SMOR) Standardized Morbidity Odds Ratio	Moderately elevated risk of colon cancer (SMOR = 1.36) and brain cancer (SMOR = 1.90). Weaker evidence of increased risk was observed for bladder cancer (SMOR=1.22), kidney cancer (SMOR=1.34) and Hodgkin's lymphoma (SMOR=1.81).
Cancer Risk Among Firefighters: A Review and Meta-Analysis of 32 Studies [64]	N/A	N/A	32 previous studies on firefighters	(SRE) Summary Risk Estimate	Probable cancer risk for multiple myeloma (SRE=1.53), non-Hodgkin lymphoma (SRE=1.51), prostate cancer (SRE=1.28), and testicular (SRE=2.02). Possible risk of skin cancer (SRE=1.39), Malignant Melanoma (SRE=1.32), Brain cancer (SRE=1.32), Rectum cancer (SRE=1.29), Buccal Cavity and Pharynx cancers (SRE=1.23), Stomach cancer (SRE=1.22), Colon cancer (SRE=1.21), Leukemia (SRE=1.14).
2022 IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 98 Painting, Firefighting, and Shiftwork [62]	N/A	N/A	Previous studies on firefighters	N/A	Occupational exposure as a firefighter is carcinogenic to humans (Group 1). There is sufficient evidence for mesothelioma and bladder cancer in humans, and limited evidence for colon cancer, prostate cancer, testicular cancer, melanoma of the skin, and non-Hodgkin lymphoma.

2.4.6. Current Fire Responder Decontamination Practices

As researchers and members of the fire service industry learn about the contaminants, exposures, and health risks associated with the fireground, decontamination and exposure mitigation strategies are becoming increasingly important to ensure workers can come home to their families at the end of their careers. The old-fashioned mentality that “dirty bunker gear is a badge of honor” is slowly being superseded with respect and an emphasis on routinely cleaning equipment and gear, reflecting a more educated industry.

The NFPA recommends that firefighters take a shower with soap and water to wash away any contaminants they were exposed to shortly after returning to the fire station. This has been popularized by members in the fire service industry as they chuckle about the “shower in the hour” catchphrase that has been popularized. After cleaning themselves, firefighters clean the individual parts of the protective ensemble that were taken to the fire scene. The NFPA also recommends that each personnel have a second set of gear to allow firefighters to respond to multiple calls without cleaning gear in between responses. Unfortunately, due to logistical and budget constraints faced by most rural and volunteer fire departments, purchasing additional sets of equipment is not always feasible. Once the firefighters themselves and their gear have been cleaned, any vehicles that were driven in contaminated environments are also washed and the air filters replaced [68].

On-scene decontamination methods are rapidly being developed and implemented by fire departments to remove contaminants from the turnout ensemble and personnel prior to transport to reduce the chance of contaminating the fire station. Popular on-scene decontamination methods include scrubbing down each firefighter with brushes and soap and water [47]. Furthermore, firefighters have begun placing their contaminated gear in an air-tight container or a garbage bag to prevent cross contamination [68, 69]. Figure 8 illustrates the wet soap brushing method a firefighter may use for on-scene decontamination. Fire departments may use various types of cleaning methods such as brush, airbrush, wet, or wet soap. No matter the method each have been found to remove contaminants from the turnout gear.

However, firefighters are a proud and perhaps stubborn group that may not always participate in decontamination procedures. A 2017 survey of South Florida fire departments found that firefighters reported positive attitudes towards clean turnout gear and believed that

cleaning their gear will reduce their risk of cancer, but there was a large disconnect between their beliefs and actions. Firefighter responses showed that showering within the hour of exposure was the only method of decontamination done routinely. Nearly 95% of firefighters claimed they never or only occasionally bagged their gear before returning to the fire station. Few firefighters, less than 20%, reported they frequently or always cleaned their gear before leaving the fire-scene or used decontamination wipes [70].

A second Florida study questioned firefighters about their decontamination practices, knowledge, confidence and showering practices. Roughly 60% of respondents said they had cleaned their turnout gear within the previous year and had responded to a fire within the same time period. Slightly over half of firefighters, 51.3%, clean their gear at the fire station and 26.6% of firefighters said they clean their gear at home most frequently [71]. The practice of cleaning turnout gear at home goes against the guidelines of NFPA 1851. These two Florida studies demonstrate that firefighters do not always follow NFPA guidelines.



Figure 8: Los Angeles County firefighters demonstrate the "On-Scene Decontamination" process [72]

Decontamination wipes provide a possible means of increasing firefighters' usage of some form of decontamination. Wipes are easy to use, store, transport, and also address several worries mentioned in the 2017 study on South Florida firefighters [71]. Baby wipes are most prominently used among firefighters, although there are several substitutes advertised towards firefighters. Fire investigators do not have the luxury of returning to a fire station after each visit to a fire scene and may visit multiple fire scenes in a single day, up to eight separate scenes in a single day. This makes on-scene decontamination more crucial and exemplifies the increased risk of cross contamination. Decontamination wipes are an option of on-scene decontamination that would easily suit fire investigators needs.

2.5. Fireground Contaminants

Soot, smoke, gases, and vapors are guaranteed to be present on the fireground because they are byproducts of combustion reactions. The specific chemicals present are dependent on the fuel source and availability of oxygen, which is unique to every fire. The list of chemicals and contaminants present at any fire scene can be upwards of hundreds if not thousands of unique chemicals. Hazardous contaminants are divided into two groups: asphyxiant gases and irritants. Asphyxiant gases deprive the blood of oxygen and restricts the oxygen supply to the brain resulting in death. Carbon monoxide and hydrogen cyanide are two asphyxiant gases that have been measured at levels capable of significant acute toxic effects and/or death on fire scenes [73, 74]. Irritants inhibit or increase the difficulty of breathing by stimulating pain receptors in the respiratory tract and can cause severe eye irritation. Common irritants include acrolein, hydrogen chloride, and particulate matter [75].

Although gaseous and vapor chemicals present serious health risks for acute and chronic exposures, they fall out of the scope of this literature review because inhalation exposure can be significantly reduced by modern respiratory equipment. The scope of this review will focus on the particulate matter, soot, smoke, and the chemicals present in these mediums and the dermal exposure associated.

2.5.1. Particulate Matter and Smoke

The National Firefighter Protection Association Standard 92, 2009 edition defines smoke as “the airborne solid and liquid particulates and gases evolved when a material undergoes pyrolysis or combustion, together with the quantity of air that is entrained or otherwise mixed into the mass.” [76]. Smoke particles can be extremely dangerous because of their microscopic

size and ability to reduce visibility and are intermixed with toxic chemicals, gases, and particulate matter. Due to their microscopic, and sometimes nanoscopic sizes particulates can penetrate the lower respiratory system causing respiratory and cardiovascular disease.

Particulate matter, a main component of smoke, is also a contaminant guaranteed to be present at a fire scene. Although the mechanism of soot particulate formation is not fully understood, there are several theories and considerable agreement on the general features of the process involved, which are summarized in Figure 9 as an introductory overview shown schematically [77, 78]. In general, there are several mechanisms that generate particulate matter with various reaction precursors. Additionally, the type of fuel can change the mechanism of particle growth, correlations between soot formation and fuel structure have been established between aromatic fuels, like benzene and acetylene and aliphatic fuels, like acetylene, ethylene, or methane [78].

2.5.1.1. Characterization

The most apparent combustion products are smoke and soot because of the dark black and gray colors as well as their abundance at a fire scene. Soot and smoke particles can range from less than 1 micrometer up to 100 micrometers in diameter, all of which pose serious health risks. As described in section 2.3.2, particulate matter is separated into one of two categories, PM₁₀ and PM_{2.5}. Regardless of the size, particulates act as vehicles for the toxic combustion chemicals produced during the fire which may adsorb onto the surface of these particulates. Toxic chemicals such as polycyclic aromatic hydrocarbons (PAHs), carbon monoxide, hydrogen cyanide, nitrogen dioxide, formaldehyde, and several other organic and inorganic compounds have been found in smoke and soot at fire scenes.

2.5.1.2. Formation and Growth Mechanisms of Particulate Matter

The foundation of several current soot formation theories stem from the “Hydrocarbon Polymerization Theory,” stated by Gaydon and is as follows,

“In the presence of an excess of fuel molecules, free radicals initiate chain polymerization processes which lead to the formation of higher hydrocarbons which decompose thermally to solid carbon and hydrogen. In the presence of sufficient oxygen, the radicals are removed by reaction with this and do not cause so much polymerization [77].”

The first step of particulate formation is the formation of the first aromatic ring, perceived to be a crucial step because it is believed to be the rate-limiting step in the reaction sequence to producing larger aromatic species.

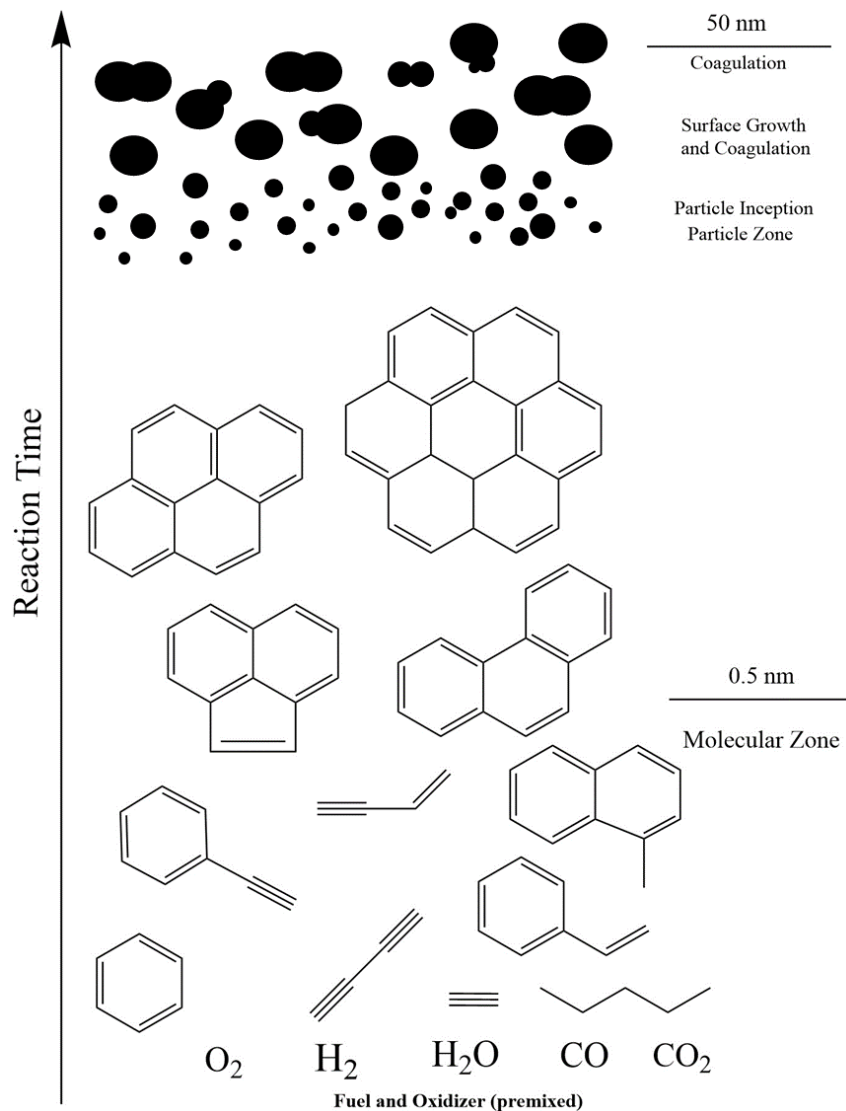


Figure 9: Illustration of the formation of particulate from molecular structures adapted from Richter and Howard 2000 [78]

There have been many theories to attempt to describe the reaction mechanism that produces the first aromatic ring, listed in Table 5. One of the earliest theories proposed was the even-carbon-atom pathway that suggested Even-Carbon-Atom Pathway played a key role in the formation of the first aromatic ring and Even-Carbon-Atom Pathway was identified to play a role at lower temperatures by numerical simulations [77]. Miler and Melius, dismissed Even-Carbon-Atom Pathway & Even-Carbon-Atom Pathway by stating that n-C₄H₃ and n-C₄H₅ could not be present in sufficiently high concentration and proposed the odd-carbon-atom pathway via combination of propargyl radicals, Odd-Carbon-Atom Pathway. Additionally, other odd-radical-pathways have been suggested, Odd-Carbon-Atom Pathway and Odd-Carbon-Atom Pathway. Another possibility for the initial ring formation is the reaction between propargyl and acetylene to form a cyclopentadiene radical, Odd-Carbon-Atom Pathway. This reaction pathway combines the highly stable radical, propargyl, and acetylene, the most abundant “building block” from the previous reaction pathways, and shows that it has an even faster rate of reaction by a factor of 2 - 10³, relative to Odd-Carbon-Atom Pathway, suggesting that this is a dominant role in the formation of the first aromatic ring [77]. Regardless of the specific reaction mechanism all these reactions suggest a general reaction mechanism, shown in Figure 10.

Table 5: List of theories on the mechanisms of the first aromatic ring in particulate formation [77]

$n\text{-C}_4\text{H}_3 + \text{C}_2\text{H}_2 \rightarrow \text{phenyl}$	Even-Carbon-Atom Pathway	Equation 1
$n\text{-C}_4\text{H}_5 + \text{C}_2\text{H}_2 \rightarrow \text{benzene} + \text{H}$	Even-Carbon-Atom Pathway	Equation 2
$\text{C}_3\text{H}_3 + \text{C}_3\text{H}_3 \rightarrow \text{benzene or}$ $\text{C}_3\text{H}_3 + \text{C}_3\text{H}_3 \rightarrow \text{phenyl} + \text{H}$	Odd-Carbon-Atom Pathway	Equation 3
$\text{C}_5\text{H}_5 + \text{CH}_3 \rightarrow \text{benzene} + \text{H} + \text{H}$	Odd-Carbon-Atom Pathway	Equation 4
$\text{C}_5\text{H}_5 + \text{C}_5\text{H}_5 \rightarrow \text{naphthalene} + \text{H} + \text{H}$	Odd-Carbon-Atom Pathway	Equation 5
$\text{C}_3\text{H}_3 + \text{C}_2\text{H}_2 \rightarrow \text{c-C}_5\text{H}_5$	Odd-Carbon-Atom Pathway	Equation 6

There have been several theories that have attempted to identify a mechanism of the first aromatic ring from acetylene and other early stage building blocks but there are other growth and formation mechanisms of particulate matter that stem from other molecular species. Proposals have included methyl, propargyl, cyclopentadienyl, and benzene as the focus of the growth

reaction characterizing the growth mechanism through reacting radicals, which generally follow the suggestion that hydrocarbons with conjugated structure and their derivatives are critical intermediates to soot nucleation stated by Glassman [79, 80].

Once the first aromatic hydrocarbon is formed, regardless of the specific mechanism, the species will begin to grow. Adding carbon and hydrogen atoms, small compounds of C_2 , C_2H_2 , or larger compounds through radical reactions, hydrogen-abstraction/acetylene-addition, ring closing, hydrogen atom migration, or atom rearrangement [77, 78]. Once the aromatic species grows large enough, five- and six-membered rings minimum, they unlock the ability to react with each other. Once the parent species grows to approximate size of $C_{30}H_{10+}$ it will begin to form a bowl shape. Eventually the species grows so large it crosses the upper threshold of chemical compound and becomes a particle.

The reaction of “soot” was historically defined as the mass accumulated in PAH species above a certain size, or the transition from gaseous species to solid particles. This was initially thought to be the result of a purely chemical growth and has been the least understood part of soot formation process. While this definition accounts for soot mass it significantly underestimates the particle size because PAH species will collide and stick together forming PAH dimers, trimers, tetramers, etc., ultimately continuing to increase in size via molecular chemical growth reactions [77]. The shape of soot particles is assumed to be spherical and will collide and coalesce completely, forming new spherical particles. An image of a smoke particle taken by transmission electron micrograph can be seen in Figure 11 and illustrates the different growth mechanisms of smoke particulates.

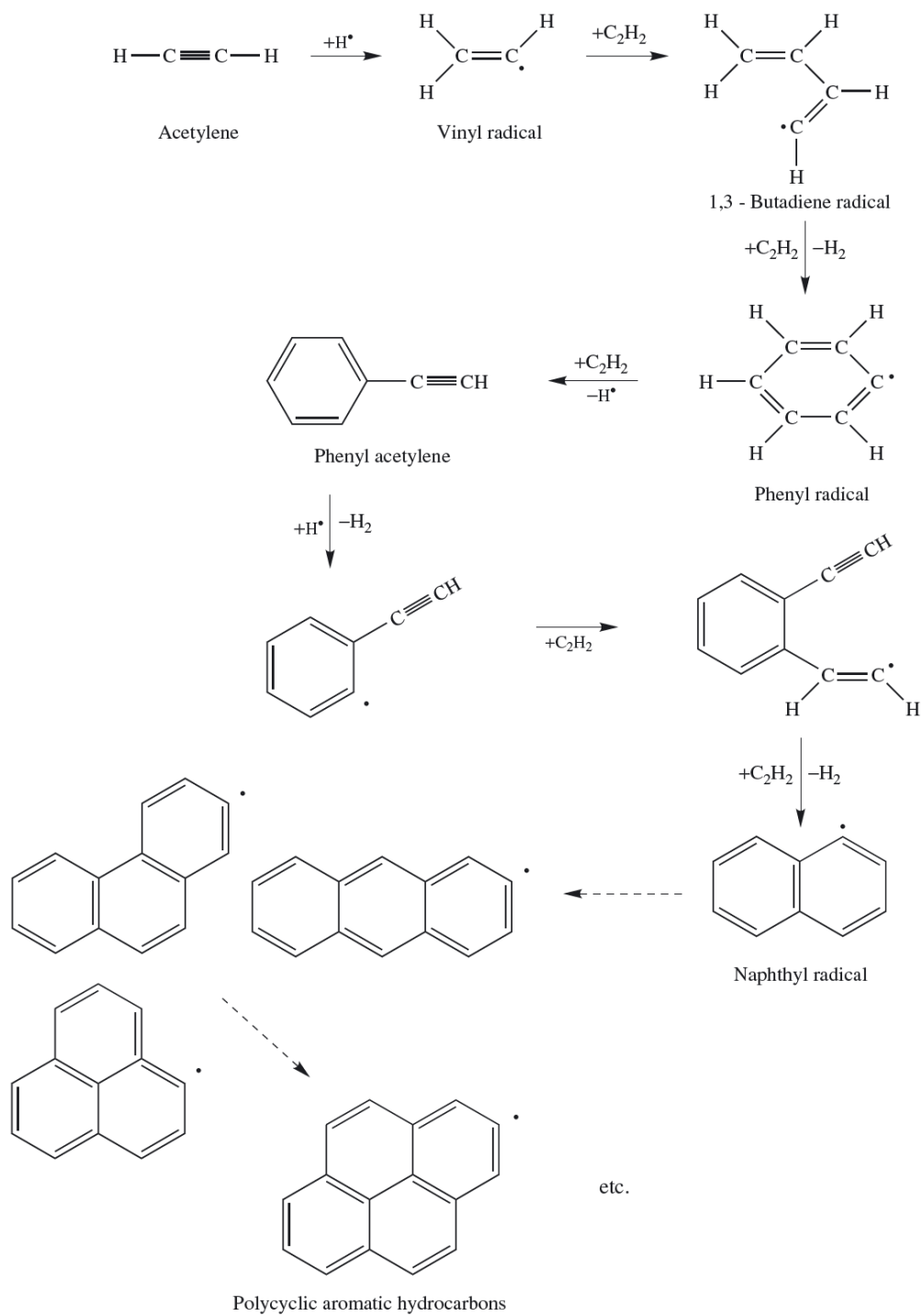


Figure 10: General mechanism of soot particle formation [78]

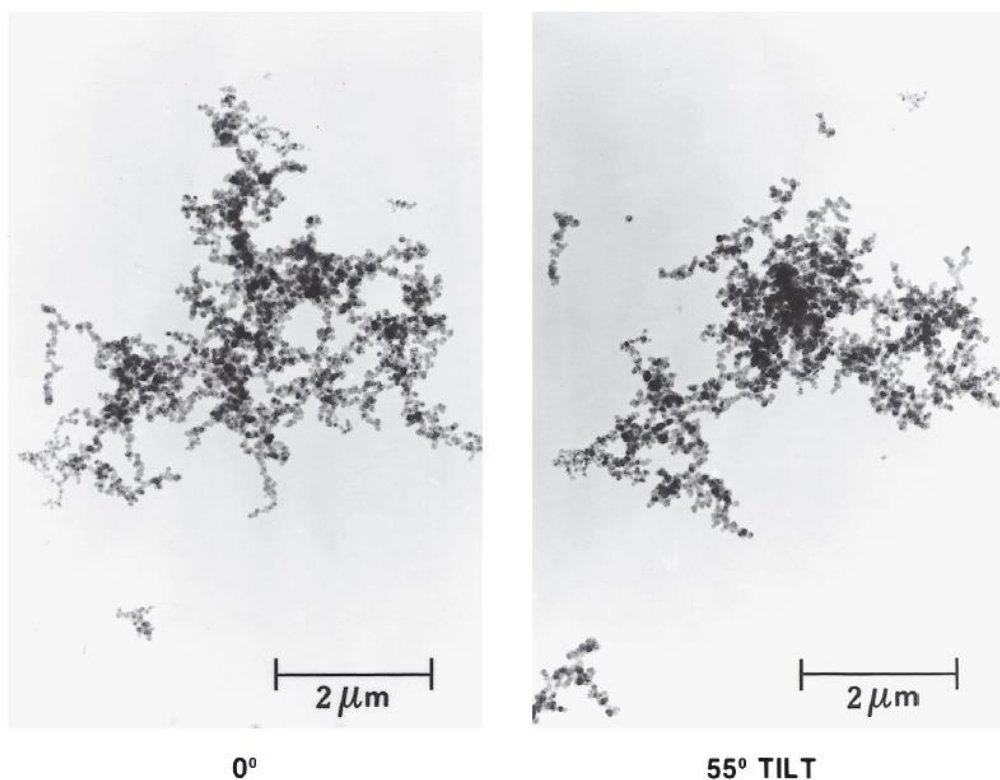


Figure 11: Transmission electron micrograph of a smoke particle. Photographs by Eric B. Steel, Chemical Science and Technology Laboratory, National Institute of Standards and Technology

Precursor reactions form the first aromatic ring, radical reactions propagate growth, once large enough soot particles can grow via particle nucleation, surface reactions, and particle coagulation. Ultimately, it is pertinent to understand that multiple growth reactions are likely to occur simultaneously to best explain the time scale of soot inception.

2.5.1.3. Smoke and Particulate Matter Health Effects and Toxicity

Smoke is one of the most well-known carcinogens and its toxicity has been researched extensively. Common regulatory practices include warning labels, increasing the cost of tobacco products through taxation, restricting advertising, limiting areas where individuals can smoke, and reducing accessibility attempt to disincentivize smoking and educate civilians. Regardless of the risks people continue to smoke and tobacco smoke is responsible for about four million deaths a year worldwide; however, these mortality numbers reflect decades old smoking patterns and do not consider the increase in global cigarette consumption over the past century [81].

Research on smoke toxicity has been continued for several decades and researchers identified 69 carcinogens in tobacco smoke by the year 2000. These 69 carcinogens include ten species of PAHs, six heterocyclic hydrocarbons, four volatile hydrocarbons, three nitro-hydrocarbons, four aromatic amines, eight N-heterocyclic amines, 10 N-nitrosamines, two aldehydes, ten miscellaneous organic compounds, nine inorganic compounds, and three phenolic compounds [82]. Since the previous IARC Monograph on tobacco smoking done in 1986 the primary focus of research has predominantly been on benzo[a]pyrene, N-nitrosamines, and aromatic amines. Animal, human, and epidemiological studies have produced mass amounts of data that repeatedly show sufficient evidence that cigarette smoke is carcinogenic. Cancers related to tobacco smoking include lung, upper aerodigestive tract (oral cancer, and cancer of the oropharynx, hypopharynx, larynx, adenocarcinoma, and esophagus), urinary bladder, renal pelvis, pancreas, stomach, liver, kidney, uterine cervix, cancers of the nasal cavities and nasal tissues, and myeloid leukemia [83].

In addition to the smoke, particulate matter is also dangerous to human health. Exposure to PM can trigger a major mechanism of cell death through inflammatory-related cascade, oxidative stress, and DNA damage [84]. Larger particles, PM₁₀, include particles 10 microns or smaller and can penetrate and lodge deep in the lower areas of respiratory system. Smaller particles PM_{2.5} include particles 2.5 microns or less and can be even more dangerous because they can penetrate the lung barrier and enter the blood system and penetrate the skin [25]. Furthermore, the chemicals adsorbed onto the surface of PM can cause further damage or cell death. Dose is an extremely crucial factor in PM exposure. Reports have shown that cytotoxic effects occur after acute exposures to high concentrations of PM₁₀ but can be avoided if exposure is minor. However, chronic exposures to lower concentrations cause repeated DNA damage and disrupts proliferation, growth, and cell death genes, resulting in increased risk of cancer. Overall, lung cancer has been strongly associated with prolonged exposure to PM [84].

2.6. Polycyclic Aromatic Hydrocarbons

2.6.1. Characterization

Polycyclic aromatic hydrocarbons (PAHs), also referred to as polynuclear aromatic hydrocarbons, are a class of organic chemicals that contains over 100 compounds [85]. For this literature review, “polycyclic aromatic hydrocarbons” will be utilized from here on out. These compounds are strictly composed of carbon and hydrogen atoms arranged in either linear,

cluster, or angular arrangements of aromatic rings. Figure 12 illustrates the 16 PAHs the U.S. Environmental Protection Agency (EPA) has deemed as priority chemicals. Priority chemicals are evaluated by the EPA based on the chemical's abundance, toxicity, and potential for exposure.

Polycyclic aromatic hydrocarbons are primarily produced as complex mixtures via the incomplete combustion of materials including crude oil, motor fuel, wood, and manufacturing processes such as the distillation process of coal into coke or coal tar and crude oil maturation. This class of chemicals is used in several applications: medicines, pharmaceuticals, dyes, pigments, plastics, and pesticides [85]. Due to the widespread use of these chemicals, and the possibility of being produced naturally, they are a persistent environmental contaminant found throughout the world and can have adverse health effects following acute and chronic exposures.

Table 6: Chemical Properties of the Environmental Protection Agency's 16 Priority PAHs

Compound	Molecular Weight (g/mol)	Number of Aromatic Rings	Boiling Point (°C)	Vapor Pressure (mmHg @ 25°C)	logP	IARC Class	CAS Number
Naphthalene	128.17	2	218.0	8.50e-2	3.30	2B	91-20-3
Acenaphthylene	152.19	3	280.0	4.80e-3	3.94	3	208-96-8
Acenaphthene	154.20	2	279.0	2.20e-3	3.92	3	83-32-9
Fluorene	166.22	2	295.0	6.00e-4	4.18	3	86-73-7
Phenanthrene	178.23	3	340.0	1.21e-4	4.46	3	85-01-8
Anthracene	178.23	3	340.0	6.53e-6	4.45	3	120-21-7
Fluoranthene	202.26	3	384.0	9.22e-6	5.16	3	206-44-0
Pyrene	202.25	4	404.0	4.50e-6	4.88	3	129-00-0
Benz[a]anthracene	228.29	4	438.0	2.10e-7	5.76	2B	56-55-3
Chrysene	228.30	4	448.0	6.23e-9	5.81	2B	218-01-9
Benzo[a]pyrene	252.31	5	495.0	5.49e-9	6.13	1	50-32-8
Benzo[b]fluoranthene	252.32	4	481.0	5.00e-7	5.78	2B	205-99-2
Benzo[k]fluoranthene	252.32	4	480.0	9.65e-10	6.11	2B	207-08-9
Benzo[g,h,i]perylene	276.33	6	550.0	1.00e-10	6.63	3	191-24-2
Dibenz[a,h]anthracene	278.35	5	524.0	9.55e-10	6.75	2A	53-70-3
Indeno[1,2,3-c,d]pyrene	276.33	6	536.0	1.25e-10	6.70	2B	193-39-5

As environmental contaminants, PAHs have been found in air with concentrations ranging 1-20 ng/m³ in Europe and 1 ng/m³ in the USA [86], soil and sediments samples ranging from 0.1 – 2225.5 µg/kg in El Paso, Texas [87], drinking water ranging from 15-844 ng/L in Henan Province, China [88]; and food where people were consuming 3µg/day/person of PAHs [89].

As pure chemicals, PAHs are mostly colorless, white, or pale yellow-green solids that can have a faint pleasant odor [90]. The class of PAHs is often split into two categories: low molecular weight, PAHs with less than four aromatic rings, and high molecular weight, those with four or more aromatic rings [91]. These two categories influence the chemical properties seen in Table 6. Smaller molecular weight PAHs tend to have low vapor pressures and low aqueous solubility, and, as PAHs increase in molecular weight these properties tend to decrease, unlike boiling point which increases [85]. Due to their inherent non-polar nature, PAHs are more soluble in organic solvents, corresponding to high octanol-water partition coefficients (K_{ow} or Log P).

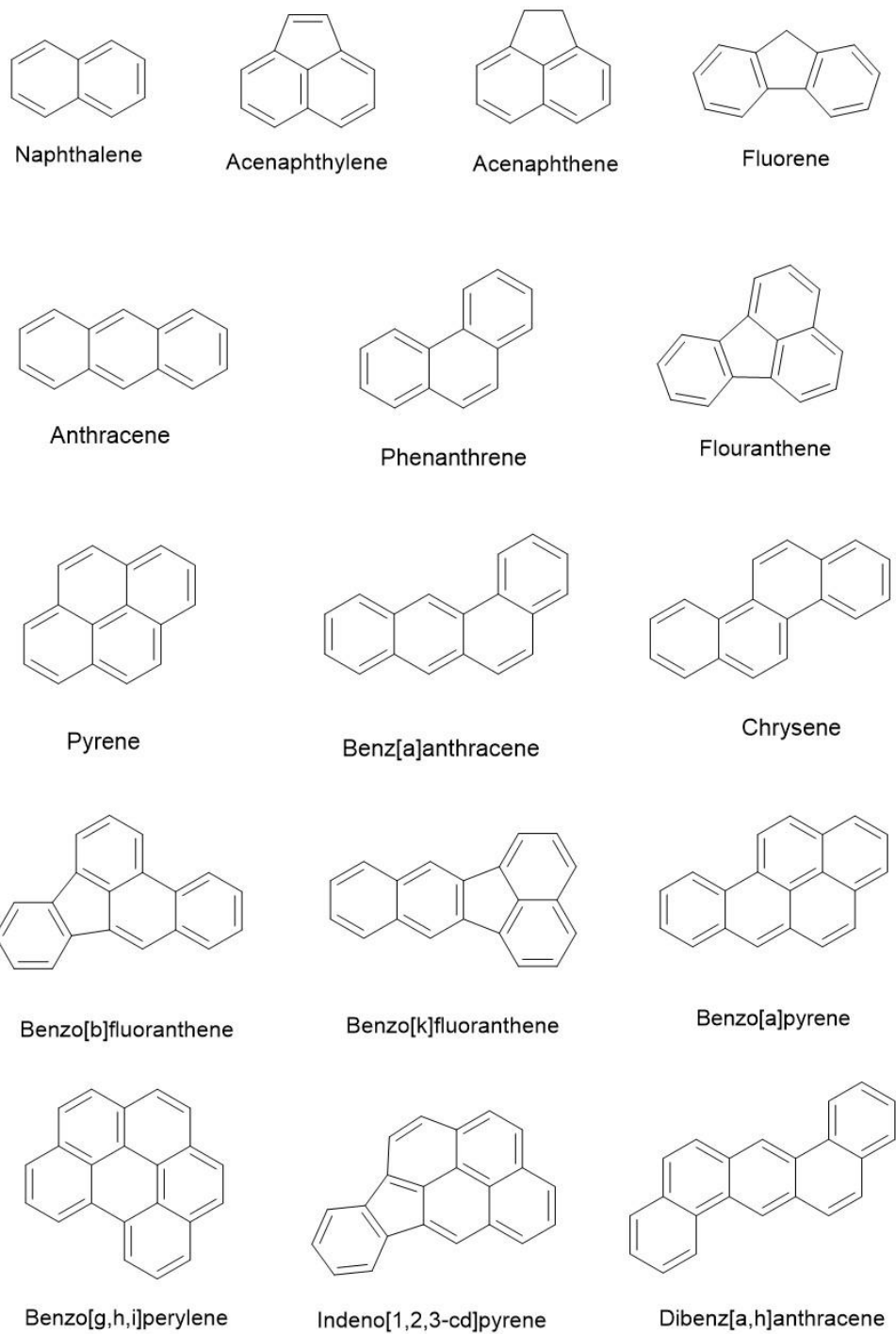


Figure 12: Chemical structures of the 16 priority EPA polycyclic aromatic hydrocarbons

2.6.2. Polycyclic Aromatic Hydrocarbon Health Effects and Toxicity

In 2015 the Agency for Toxic Substances and Disease Registry (ATSDR) ranked the entire class of PAHs 9th on their Priority List of Hazardous Substances. Meanwhile, seven individual PAHs ranked in the top 100 chemicals of the 2017 National Priorities List set by the EPA. Benzo[a]pyrene ranked 8th, benzo(b)fluoranthene ranked 10th, dibenzo(a,h)anthracene ranked 15th, benzo[a]anthracene ranked 38th, benzo[k]fluoranthene ranked 61st, benzo[b]fluoranthene ranked 73rd, and naphthalene ranked 80th [91]. Table 7 shows the carcinogenicity of PAH compounds according to the US Department of Health and Human Services (HHS), IARC, and U.S. EPA. Even though each agency has their own classification system, there is a consensus that benzo[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[a]pyrene, chrysene, dibenzo[a,h]anthracene, and indeno[1,2,3-c,d]pyrene are of concern for carcinogenicity. However, PAHs listed in the *not classifiable as to human carcinogenicity* category are subject to change as more testing is conducted and additional data are collected.

Several studies have indicated that PAHs are toxic and induce serious health effects following acute and chronic exposures. Reports have shown PAHs to cause impaired lung function in asthmatics and thrombotic effects in people affected by coronary heart disease [92]. Occupational exposures to elevated levels of individual PAHs have resulted in symptoms such as eye irritation, nausea, vomiting, diarrhea, and confusion, while mixtures of PAHs are known to cause skin irritation and inflammation [93]. The acute health effects of PAHs are essential to consider, but chronic toxicity is more relevant to firefighter health and will be further explored.

Studies on chronic exposure to PAHs have indicated a plethora of health effects. Some studies have shown that the exposure pathway is a key component when considering which type of cancer forms, in both human and animals [94]. Animal studies have shown adverse reproductive and developmental effects from PAH exposure, but similar effects have not been found in humans [95].

Toxicological studies done by ATSDR have evaluated the carcinogenicity of each exposure pathway of the 16 priority EPA PAHs along with benzo[e]pyrene. Inhalation studies on animals exposed to benzo[a]pyrene found dose-dependent relationships in producing lung tumors. Oral exposure studies found that high doses of benz[a]anthracene, benzo[a]pyrene, and dibenzo[a,h]anthracene are carcinogenic to rodents. Dermal exposure studies have displayed the

capability of benz[a]anthracene, benzo[b]fluoranthene, benzo[j]fluoranthene, benzo[a]pyrene, chrysene, dibenz[a,h]anthracene, and indeno[1,2,3-c,d]pyrene to induce skin tumors in laboratory animals [94].

Table 7: PAH carcinogenicity according to the U.S. Department of Health and Human services, International Agency for Research on Cancer (IARC), and U.S. Environmental Protection Agency (EPA) [92]

U.S. Agency	PAH Compound(s)	Carcinogenic Classification
U.S. Department of Health and Human Services	Benz[a]anthracene	Known Animal Carcinogen
	Benzo[b]fluoranthene	
	Benzo[a]pyrene	
	Dibenz(a,h)anthracene	
	Indeno(1,2,3-c,d)pyrene	
International Agency for Research on Cancer (IARC)	Benz[a]anthracene	Probably Carcinogenic to Humans
	Benzo[a]pyrene	Possibly Carcinogenic to Humans
	Benzo[a]fluoranthene	
	Benzo[k]fluoranthene	
	Indeno(1,2,3-c,d)pyrene	Not Classifiable as to their Carcinogenicity to Humans
	Anthracene	
	Benzo[g,h,i]perylene	
	Benzo[e]pyrene	
	Chrysene	
	Fluoranthene	
	Fluorene	
	Phenanthrene	
	Pyrene	
U.S. Environmental Protection Agency (EPA)	Benz[a]anthracene	Probable Human Carcinogen
	Benzo[a]pyrene	
	Benzo[b]fluoranthene	
	Benzo[k]fluoranthene	
	Chrysene	
	Dibenzo[a,h]anthracene	
	Indeno[1,2,3-c,d]pyrene	Not Classifiable as to Human Carcinogenicity
	Acenaphthylene	
	Anthracene	
	Benzo[g,h,i]perylene	
	Fluoranthene	
	Fluorene	
	Phenanthrene	
Pyrene		

Unexpectedly, the PAH compounds themselves are not carcinogenic but rather the metabolite byproduct produced when PAHs are metabolized by the body. Of the 16 priority PAHs, the metabolism of benzo[a]pyrene is used as an exposure marker for the assessment of the carcinogenicity of PAH mixtures [96]. When benzo[a]pyrene is absorbed into the body, it is metabolized by three major pathways: 1) CYP1A1/1B1 and Epoxide Hydrolase pathway, 2) CYP Peroxidase pathway, and 3) Aldo-Keto Reductases pathway [97]. The CYP1A1/1B1 and Epoxide Hydrolase pathway will be highlighted in this literature review and is shown in Figure 13.

When PAHs, like benzo[a]pyrene, enter the body they bind to aryl hydrocarbon receptors (AHRs) found in common cells. When a PAH binds to an AHR it induces production of metabolic enzymes, cytochrome P450s (CYPs), to metabolize the PAH. Cytochrome P450s are a group of enzymes in the body that react with drugs, xenobiotics, and other compounds to increase the hydrophilicity of a compound by adding reactive groups. In the CYP1A1/1B1 and Epoxide Hydrolase pathway, CYPs will add an epoxide group to benzo[a]pyrene, which is then catalyzed by epoxide hydrolase to create hydroxyl groups on benzo[a]pyrene, forming benzo[a]pyrene-7,8-diol [98]. Epoxide and hydroxyl groups are extremely reactive and capable of reacting with cells and DNA. The metabolite, benzo[a]pyrene-7,8-diol, can react with CYPs enzymes again to form the ultimate carcinogen benzo[a]pyrene-7,8-diol-9,10-epoxide [98]. Once in this form, the benzo[a]pyrene metabolite can easily react with DNA producing DNA adducts that cause cancer. Benzo[a]pyrene can undertake multiple metabolic pathways creating various metabolites. Out of these metabolites, the isomer (+)-benzo[a]pyrene 7,8-diol-9,10 epoxide is extremely reactive with significant carcinogenic potential and is referred to as the “ultimate carcinogen” [99].

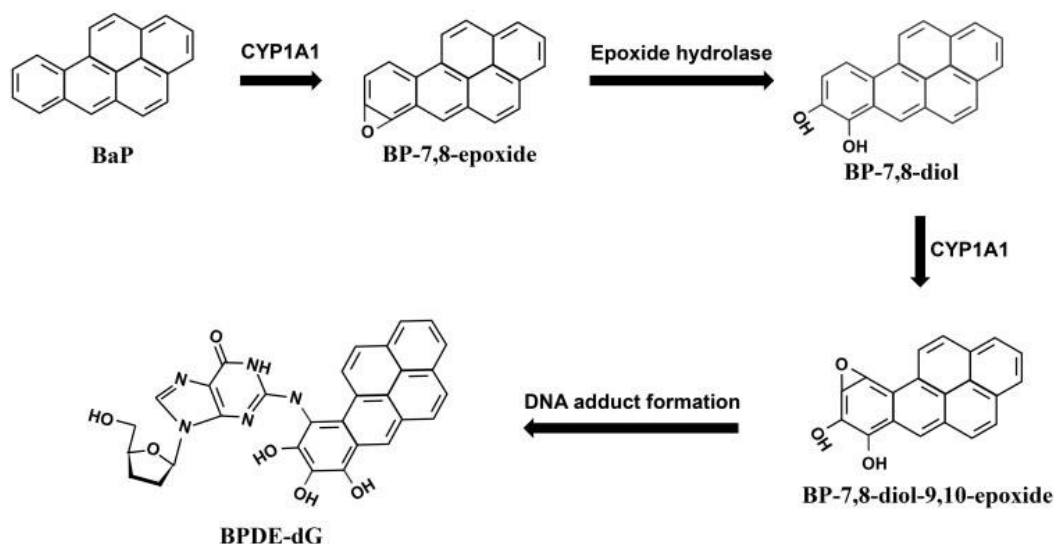


Figure 13: Illustration of the metabolic reaction of Benzo[a]pyrene into Benzo[a]pyrene-7,8-diol-9,10-epoxide via the CYP1A1/1B1 pathway [97]. The parent compound benzo[a]pyrene is metabolized by cytochrome P450s, which will add an epoxide group to benzo[a]pyrene to increase its hydrophilicity to remove the chemical from the body, forming BP-7,8-epoxide. BP-7,8-epoxide is then catalyzed by epoxide hydrolase to create hydroxyl groups in place of the epoxide group. BP-7,8-diol can react with the CYPs a second time, again adding an epoxide group. The final product BP-7,8-diol-9,10-epoxide is extremely reactive and can react with DNA creating DNA adducts [98].

2.6.3. Dermal Absorption Studies

The dermal absorption of PAHs has been thoroughly studied in humans and animals. Studies have tested the absorption across several laboratory animal species, including mice, rats, monkeys, and guinea pigs, as well as humans in occupational exposure studies [100, 101, 102, 103, 104, 105]. These studies have examined individual or complex mixtures of PAHs to assess the penetration capabilities or effects of mixtures on dermal absorption. Percutaneous absorption of PAHs appears to be rapid in both humans and animals. However, the extent of absorption is variable among PAH compounds and may be affected by the dosing vehicle used to expose the test subject [94]. Additional factors, including the anatomical site of application, animal species, skin temperature, hydration of the skin, and physicochemical properties of the chemical, can influence dermal absorption [106].

Dermal absorption studies on mice, rats, monkeys, and guinea pigs have shown the percutaneous absorption of [¹⁴C]-benzo[a]pyrene to be “quick and high” [103, 104, 105]. A study by Ng and coworkers tested the dermal absorption of pyrene and benzo[a]pyrene *in vivo* and *in*

vitro using high and low dose amounts with hairless guinea pigs. *In vivo* results indicated that benzo[a]pyrene penetrated the skin slower than pyrene, where 34% of the dose was absorbed and eliminated in twenty-four hours and 73% of the dose absorbed and eliminated in seven days. *In vitro* tests demonstrated comparable results with 67% absorption of the administered dose in twenty-four hours. A noticeable finding was when the dose was increased five-fold, it produced double the of metabolites [105].

Nowadays, human subject studies are rare. Current human subject testing standards prioritize minimization of health risks for study participants so studies relating to biological interactions with carcinogens have been restricted. However, older studies conducted before new regulations and standards were implemented can provide critical insight. Storer and coworkers applied 2% coal tar mixture to the skin of humans for 8-hour periods for two consecutive days and found detectable levels of phenanthrene, anthracene, pyrene and fluoranthene in the blood [107]. Surprisingly, benzo[a]pyrene was not detected in the blood but was present in the coal tar mixture. However, during the time that this study took place biomonitoring techniques were not capable of analyzing the benzo[a]pyrene metabolites that were likely present in the blood, thus, allowing benzo[a]pyrene to go undetected.

Van Rooij and coworkers applied coal tar to the skin of volunteer at various anatomical sites examined the surface disappearance of PAHs and monitored the excretion of PAH metabolites to determine PAH absorption at different anatomical sites. The study reported low but significant differences in dermal absorption between anatomical sites: shoulder > forehead, forearm, groin > ankle, hand by monitoring the surface disappearance [100]. Differences in absorption based on anatomical site is to be expected as skin thickness is not consistent across the body. Areas of the body subject to repeated abrasion, such as the soles of the feet and palms of the hand, have the thickest skin. Areas that contain sweat glands, hair follicles, or sebaceous glands typically have thin skin [108].

Another occupational exposure study done by Van Rooij and coworkers examined the dermal uptake of pyrene in twelve coke plant workers [109]. Exposure pads were placed at the jaw/neck, shoulder, upper arm, wrist, groin, and ankle to record the skin contamination of pyrene during five consecutive 8-hour shifts. The contamination of the exposure pads ranged from 21 μg to 166 μg per day, and biological samples reported dermal uptake to be 4 – 34 $\mu\text{g}/\text{day}$, roughly 20% of the pyrene contamination on the skin. Personal air samples had an average concentration

of pyrene of 0.1 – 5.4 µg/m³ and the average respiratory uptake was estimated to be 0.5 – 32.2 µg/day. Based on the estimated dermal and inhalation exposure the study concluded that an average of 75% of the total absorbed amount of pyrene to be attributed to dermal absorption [109].

These studies show the importance of how and where penetrating chemicals encounter human skin. Van Rooij and coworkers found that different anatomical sites have varying degrees of chemical absorption due to the differences in epidermal skin thickness. Van Rooij's study with coke plant workers exemplified how people are at risk of dermal absorption and inhaling chemicals when working near combustion sources [109]. Firefighters should be less concerned with inhalation exposure as long as they wear their SCBAs.

However, the data collected from dermal absorption studies that use animal skin can only estimate human dermal absorption. Studies using human cadaver skin or monitor exposure through chemical metabolites and other biological indicators would be more indicative of human absorption. Animal dermal studies should be used to determine if chemicals have the potential to penetrate human skin. Without sufficient animal testing the quickest way to determine a chemicals ability to penetrate human skin is to use human skin, which is difficult to obtain.

2.6.4. Firefighter Exposures to Polycyclic Aromatic Hydrocarbons

Firefighting is an occupation that has similar exposure rates to those occupations with the highest exposure rate to PAHs. Like most occupations that work closely to combustion sources, exposure to PAHs is most common through either inhalation or dermal exposure, through contact with contaminated clothing or chemicals deposited directly on the skin. Additionally, exposures are extremely variable between individuals.

A study on the PAH exposure of aluminum production workers found different exposures depending on workers' duties. Those who are associated with Soderberg electrolysis have about ten times higher PAH exposures than those in other departments [110]. This variability with the job duty remains true for firefighters as well. The job assignment of a firefighter can affect their proximity to the smoke produced and, ultimately, the level of PAH contamination they can encounter. Fent and coworkers showed that firefighters tasked with going inside a structure during fire response had higher levels of PAH contamination than firefighters who never entered the burning structure [47].

The City of Phoenix Fire Department characterized firefighter exposure during fire suppression activities and overhaul phase for 25 structural fires. Across these 25 fires published ceiling values were exceeded by carbon monoxide at 5 fires, formaldehyde at 22 fires, and glutaraldehyde at 5 fires. Published short-term exposure limit values were exceeded by benzene at 2 fires, NO₂ at 2 fires, SO₂ at 5 fires. Out of the 88 total PAH samples three compounds: acenaphthylene (n=34), naphthalene (n=28), and phenanthrene (n=13), were consistently found to be above the limit of detection. All other PAHs had five or fewer samples above the limit of detection. However, when summed together the total PAH concentration exceeded the NIOSH recommended exposure limits (0.1 mg/m³) for coal tar pitch volatiles at 2 fires [24].

A Swedish study investigated the chemicals in the emissions produced during automobile fires. Inorganic compounds, volatile organic compounds, isocyanates, and PAHs were all found in the gases produced during the fire. The total amount of PAHs found for the duration of the test series was 119 grams, where smaller PAHs like naphthalene and acenaphthene were most abundant and particle bound PAHs totaled approximately 8% of the total [111]. The production of particle-bound PAHs greatly increased after 60 minutes, seen in the top image of Figure 14. During the extinguishment of the automobile the total PAH production drastically increased, seen in the bottom image of Figure 14.

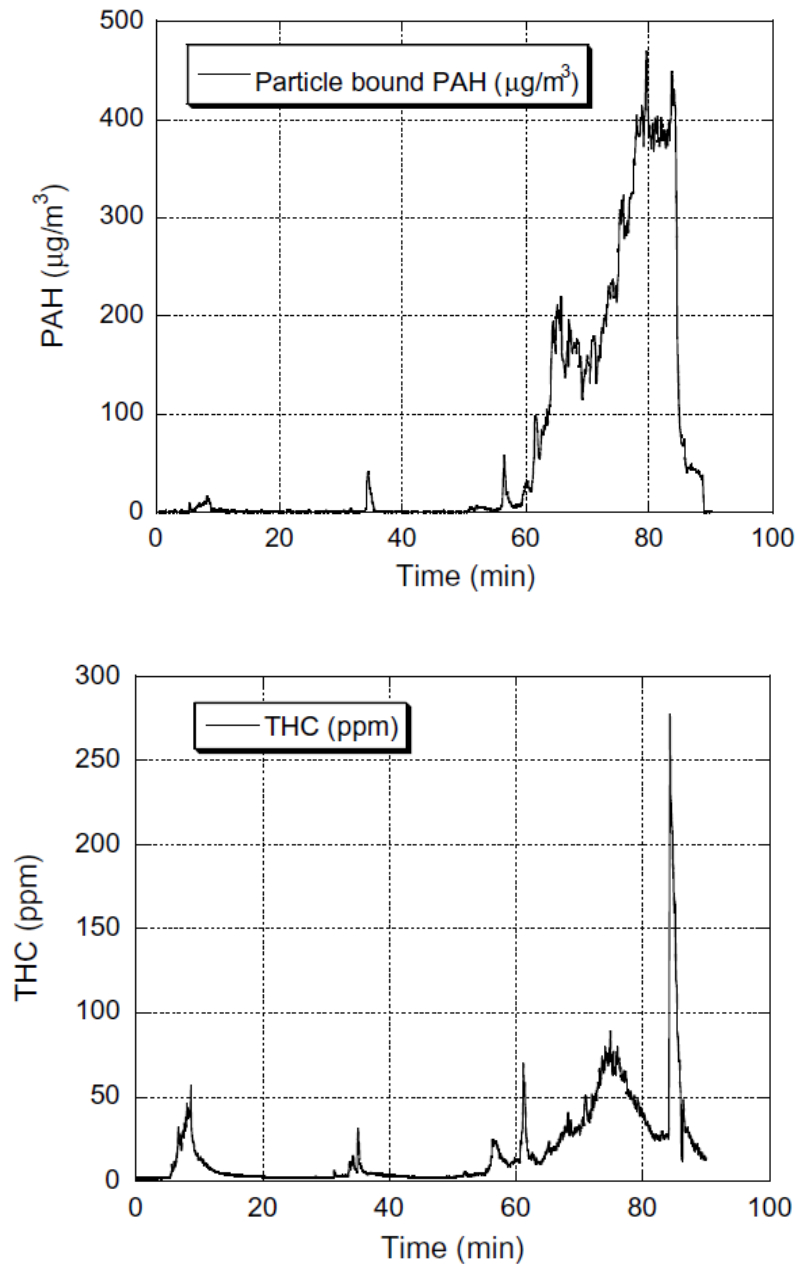


Figure 14: The top image shows the production of particle bound PAHs during automobile fires collected from the smoke gas duct. The bottom shows the Total PAH concentration during the automobile fires collected from the smoke gas duct [111].

An Australian firefighter instructor study measured the atmospheric concentrations of PAHs outside and inside the structural firefighting ensembles worn by instructors, during five live fire training cycles. Total PAH concentrations ranged from $430 \mu\text{g}/\text{m}^3$ – $2700 \mu\text{g}/\text{m}^3$ outside the instructors' firefighting ensemble and $32 \mu\text{g}/\text{m}^3$ – $355 \mu\text{g}/\text{m}^3$ inside the ensemble.

Benzo[a]pyrene concentrations ranged from $4.4 \mu\text{g}/\text{m}^3 - 63 \mu\text{g}/\text{m}^3$ and $0.6 \mu\text{g}/\text{m}^3 - 17 \mu\text{g}/\text{m}^3$, outside and inside the instructor firefighting ensemble, respectively [52].

In reviewing the previous firefighter exposure studies, those that collected air samples found increased concentrations of the smaller PAHs (naphthalene, acenaphthylene and phenanthrene) [24, 52, 111]. This is expected as the smaller PAHs have lower vapor pressure and boiling points. The variability in contaminant levels and risk for exposure between fires was perfectly exemplified by the City of Phoenix Fire Department study. The study by Lonnermark and Blomqvist showed the production of particle-bound PAHs began after 60 minutes of continuous burning and fire response activities (i.e. fire suppression) can drastically increase the production of PAHs, refer to Figure 14 [111]. As the time to reach flashover in modern structures occurs in less than four minutes, it is not irrational to believe that particle-bound PAH production occurs faster in structural fires than automobile fires. The study by Kirk and Logan found concentrations of PAHs inside the turnout jacket of firefighter instructors [52], thus reinforcing the fact that small particles can penetrate firefighter turnout gear and deposit on the skin, further demonstrating the need for blocking layers in turnout gear.

There are fewer skin sampling studies than air monitoring studies that measure firefighter chemical exposures. Two studies that have used wipe sampling to assess firefighter skin and PPE contamination found PAHs on both the skin and turnout ensemble. The NIOSH study found that wipe samples collected from firefighters assigned with different tasks had different quantities of PAHs on their turnout jackets. Inside attack and inside search had significantly more PAH contamination than overhaul or outside assignments after a single fire exposure and PAH levels on turnout gear increased with each fire response, showing that PAHs can accumulate on firefighter gear. Discrepancies in exposure between assignments/roles were supported by Fent and coworkers [47].

Although both studies show wipe sampling can be used for PAH exposure assessment there are some concerns. The wipes (Allegro® 1001) used in the Fent and coworkers study had no known collection efficiency for PAHs. This is consistent among several wipes that have been used to collect PAHs from the skin of people, largely due to no standardized test method. It is unknown if the collection efficiency is low or high, if low then all reported findings for skin samples could ultimately underestimate the dermal exposure firefighters have to PAHs and other combustion products. One consistency in both studies was that samples were collected from the

neck and hands, which were shown to be primary areas of concern in the 2015 fluorescent particulate study.

2.7. Human Skin and Skin Surrogates

During fire response, firefighters are at risk of incurring burns from the thermal hazards of a fire. Their skin is almost guaranteed to be sweating as their body responds to the extreme stimulus. Meanwhile fire investigators' skin is normally less covered as they can afford to wear more comfortable clothing. Regardless of the activities a firefighter or fire investigator may do their skin will likely encounter a chemical threat with the current level of protection provided by their personal protection equipment.

2.7.1. Structure and Function of Human Skin

Human skin is the largest organ of the human body, and acts as a barrier to the environment, toxicants, and contaminants. The skin's primary functions are to protect the body against foreign microorganisms, toxic agents, ultraviolet radiation, and maintain homeostasis by regulating the transport of water, electrolytes, and heat [112].

The skin is divided into three layers, shown in Figure 15, the most external layer being the epidermis followed by an underlying dermis layer and the innermost layer being the hypodermis layer. The epidermis, approximately 100 μm thick, is further broken down into four layers: stratum corneum, stratum granulosum, stratum spinosum, and the stratum basal layers. All together the layers of the epidermis are responsible for protecting the body against xenobiotics, ultraviolet radiation, chemical compounds, while also maintaining skin hydration, and providing mechanical resistance to minor abrasions and cuts [113, 114]. The primary barrier to the environment is the stratum corneum (SC), which is the outermost layer of the epidermis composed of dead epidermal cells that are stacked 10 – 25 layers thick which is about 10 – 40 μm [113]. The layers underneath the SC are considered viable epidermis and generate a new cell layer about once per day. This continuous replacement allows the dead cells of the SC to shed and maintain its thickness. The dead cells of the stratum corneum are held together by lipids, primarily triglycerides, fatty acids, cholesterol, and phospholipids, giving the stratum corneum its lipophilic properties [114, 115]. The structure of the stratum corneum can be analogous to a brick wall, the corneocytes analogous to bricks, surrounded and held together by a lipid-rich matrix, similar to a brick and mortar structure, seen in Figure 16 [114].

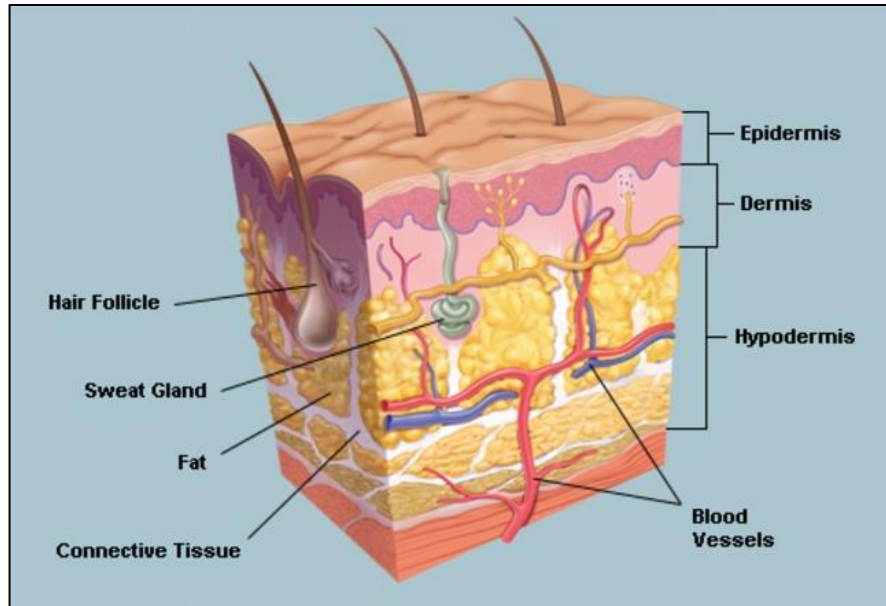


Figure 15: Structure of Human Skin detailing the Epidermis, Dermis, and Hypodermis layers [116]

The dermis, the layer of skin below the epidermis, is a collagenous and hydrous tissue that provides the skin with elasticity, flexibility, plasticity, structural support, and tensile strength, while also providing nutrients and immunological support to the epidermis [114]. This layer is highly vascular and provides ample opportunity for absorption into the body [117]. Finally, the subcutaneous hypodermis is the deepest layer of the skin and is made of loose connective tissue and fat, accounting for roughly 50% of a person's body fat. This layer provides insulation, energy metabolism, and padding.

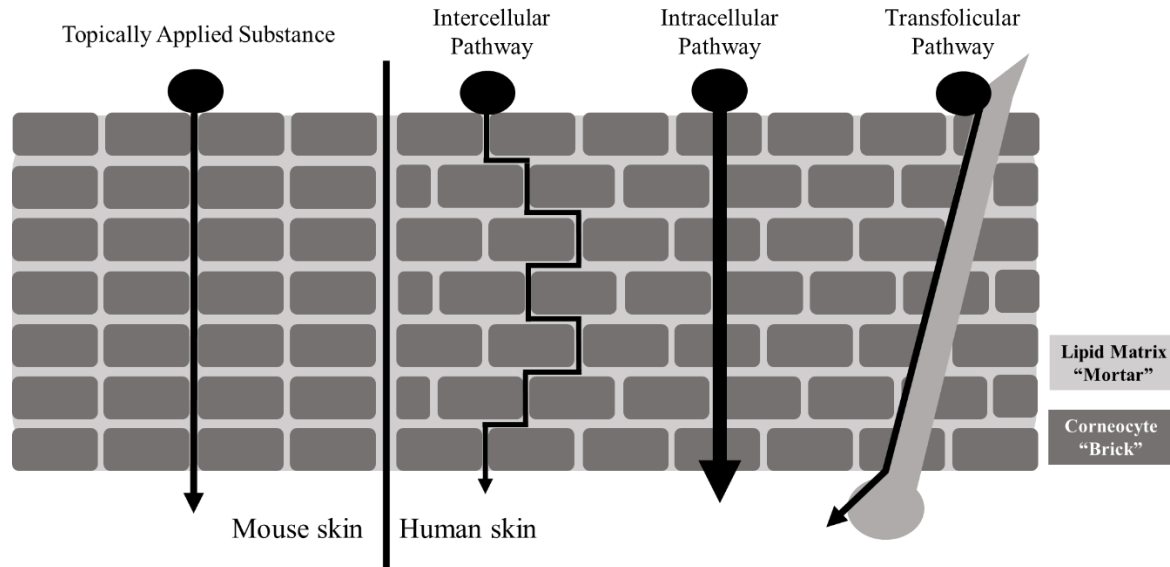


Figure 16: Schematic representation of the “Brick and Mortar” arrangement of corneocytes in mouse and human stratum corneum. The arrangement of the corneocytes create a long path for intercellular route, while transcellular and transfollicular routes are also shown [114]

Although the epidermis acts as a protective barrier, there are some areas of the body more susceptible to chemical absorption. The thickness of the epidermis is a crucial factor in preventing chemicals from penetrating the skin. Anatomical regions that are subject to repeated abrasion, such as the palms of the hands and the soles of the feet, have increased epidermal thickness [114]. Other areas of the body, such as the cheek, groin, and back, have similar epidermal thickness but have different skin permeability to chemical penetrants. In the case of firefighter skin contamination, the neck, hands, calf, and upper leg area were found to be most susceptible to particulate deposition [49]. Additionally, firefighters can contaminate themselves by touching vulnerable areas of the body with dirty hands.

2.7.2. Dermal Absorption

2.7.2.1. Absorption Pathways

Although the stratum corneum is an excellent barrier to several chemicals because of its inertness and structure, there are three primary pathways for chemicals to penetrate the stratum corneum and become bioavailable for systemic absorption. These three pathways are the intercellular route, transcellular route, and interfollicular/transfollicular route, as shown in Figure 16 [113, 114].

The intercellular route is the most tortuous as penetrating compounds must diffuse through the lipids in between the corneocytes of the stratum corneum [117]. The transcellular route is the passage through the skin barrier by diffusing through both corneocytes and the lipid matrix. Both the intercellular and transcellular routes are known as bulk pathways. The final pathway is the interfollicular also known as the transfollicular route where a compound travels down shunts provided by hair follicles, sweat glands, and sebaceous glands into the dermis [113]. This pathway is often regarded as a minor pathway because of the minimal surface area the hair follicles, sweat glands, and sebaceous glands occupy in relation to the skin [113, 117]. The absorption that occurs due to the interfollicular pathway could be described by draining an Olympic size pool using a handful of plastic straws.

The three routes of percutaneous absorption, previously mentioned, apply to healthy skin, but additional routes can be created when the skin is damaged. In an event that damages or kills skin cells, xenobiotic or chemical penetrants will have fewer layers of skin to penetrate, resulting in decreased resistance and increased absorption. Examples of damaged skin include sunburns, lacerations, abrasions, and puncture wounds. In general, dermal absorption concepts are applied to healthy full-thickness skin; however, it is important to note that absorption can be increased if the skin is impaired [114, 118].

2.7.2.2. Mechanism of Dermal Absorption

Each day people may encounter hundreds if not thousands of xenobiotics, environmental contaminants, or chemical compounds in various vehicles. A compound that comes into contact with the skin can have one of many types of interactions, which are summarized by Figure 17. Chemicals can evaporate from the surface of the skin, partially penetrate the skin stopped through metabolism or an irreversible binding reaction, or fully penetrate the skin and get fully absorbed into the body. There are several factors that will determine the degree of chemical penetration into the skin, which will be discussed later in this section. There are three groups of factors that play a significant role in dermal absorption: properties of the skin, the penetrant chemical, and external factors which may include the dose vehicle, use of chemical enhancers, or relative humidity. The overall process of chemical absorption through the skin is a passive process and can be broken down into three stages.

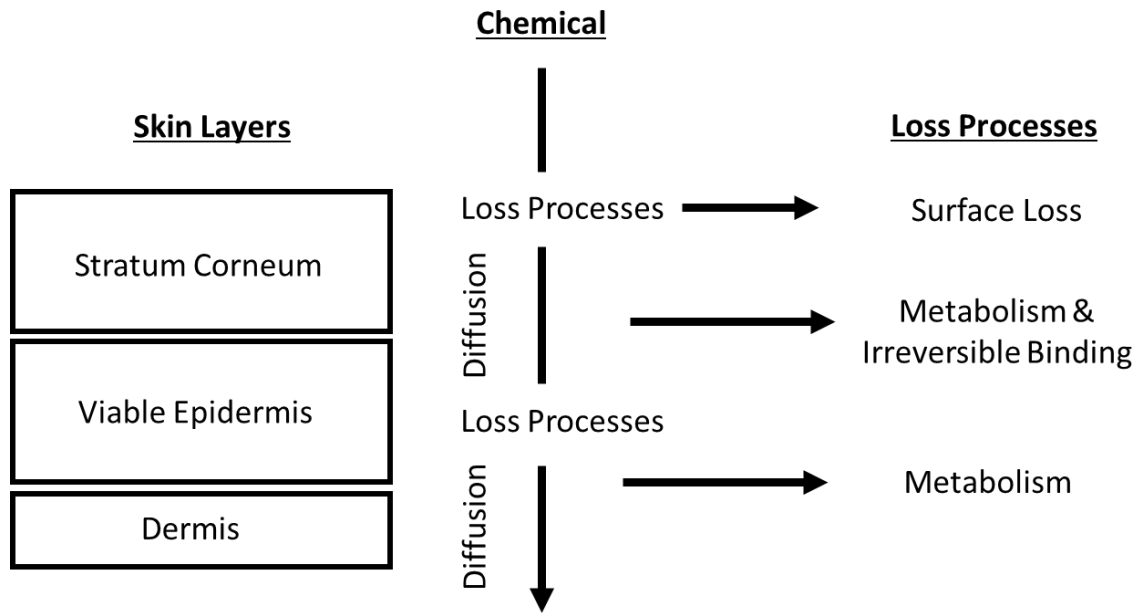


Figure 17: Illustration of dermal transport and loss processes occurring in the skin (adapted from Guy and Hadgraft (1989) [119])

The first stage of chemical absorption is contact. The penetrating chemical may come in many forms: as a pure solid, liquid mixture, moisturizer, or cream; or, in the case of fire responders, as a gas, vapor, or particulate matter deposited on the skin. If the penetrant chemical is in a solution or media that helps apply the chemical to the skin (e.g., in a controlled laboratory setting) it is referred to as the dosing vehicle. At the fire scene a common dosing vehicle would be carbon particles. When the dosing vehicle containing a chemical meets the skin contact has been made and the second stage of dermal absorption begins.

The second stage of dermal absorption is diffusion. After the chemical encounters the skin a pathway is needed to penetrate the layers of skin. If the penetrating chemical is applied to the skin using a dosing vehicle, the chemical needs to have a higher affinity for the skin otherwise it will remain in the dosing vehicle and not penetrate the skin [114]. If the penetrating chemical is successful in diffusing through the layers of the skin, then the third stage of dermal absorption follows.

The third stage of dermal absorption is absorption of the chemical into the body. If the chemical has successfully penetrated the stratum corneum and subsequent layers, it will eventually reach the underlying dermis. The dermis provides significantly less resistance to chemical penetration and, as such once the chemical has fully penetrated the stratum corneum it will likely be absorbed into the body by the capillary loops where the epidermis and dermis

layers meet [117]. If the chemical is absorbed into the blood stream it can be transported throughout the body and either become metabolized and excreted from the body or accumulate in an area of the body.

2.7.2.3. Ficks Law of Diffusion

Dermal absorption is a passive process where chemicals pass through the skin layers via diffusion. Theoretical equations and models have been developed to predict a chemicals ability to penetrate the skin. These theoretical predictions are based on Fick's laws of diffusion. Fick described the diffusion of a compound across a membrane by transforming Fourier's Law of Thermal Diffusion, a thermodynamic model of the transfer of heat by conduction, into a model of an infinite dose, shown in Equation 7, where J is the rate of transfer per unit area or flux, δC is the change in concentration, δx is the change over a distance and D is the diffusion coefficient. The negative sign indicates that the transfer of the penetrant into the skin.

Equation 7 Fick's Law of Diffusion for Infinite Dose [113]

$$J = -D \frac{\delta C}{\delta x}$$

In most dermal absorption experiments the chemical of interest is applied to a skin sample within a dosing vehicle. Initially, the chemical has the highest concentration in the dosing vehicle (C_v) relative to that of the skin and over time, the penetrating chemical permeates into the skin represented by the distribution coefficient (K_m). As mentioned previously, the thickness of the skin is not consistent across the body and inherently affects dermal absorption and is described by (h). The flux at a steady-state (J_{ss}) is given in Equation 8, where D is the diffusion coefficient, K_m is the distribution coefficient, C_v is the concentration of the chemical in the dosing vehicle. The steady-state flux across a membrane can be written in an alternate form in terms of the permeability coefficient (K_p), shown in Equation 9. Flux is a crucial measurement for dermal absorption studies because it is used as a predictor for transdermal delivery to systemic circulation.

Equation 8: Flux at steady state for a membrane

$$J_{ss} = D * K_m * C_v/h$$

Equation 9: Alternate form of Flux at steady state for a membrane

$$J_{ss} = K_p * C_v$$

The steady-state flux (J_{ss}) and permeability coefficient (K_p) are determined from in vitro experiments where an infinite dose (i.e. the concentration of the penetrating compound is maintained) is applied to the test membrane and a receiving well under the skin is constantly renewed with fresh receiving fluid acting as a sink. Over time, the flux approaches a steady-state and produces a linear curve. The time until steady-state conditions are met is known as the lag time, as seen in Figure 18, which illustrates the relationship between the cumulative mass penetrating a membrane area M_{out}/A and the steady state flux J_{ss} , permeability coefficient K_p , and lag time t_{lag} [113].

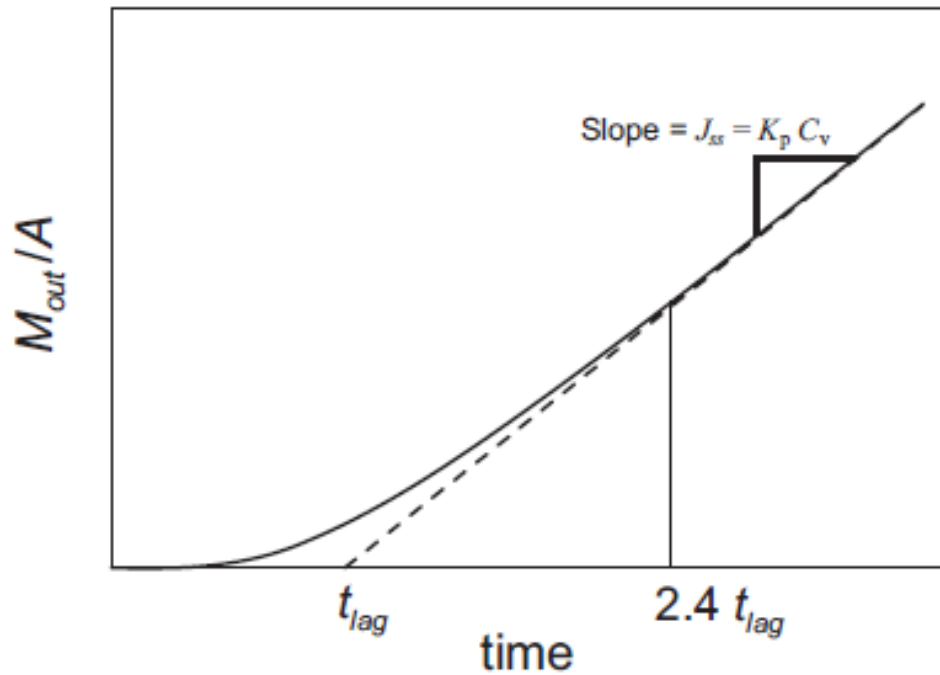


Figure 18: Illustration of the relationship between the cumulative mass penetrating a membrane area M_{out}/A and the steady-state flux J_{ss} , permeability coefficient K_p , and lag time t_{lag} [113]

Infinite dose experiments rarely represent occupational exposures scenarios because occupational exposures are limited by the work shift of a worker. These exposures may occur in swimming pools, bathing water, or any other scenario where the concentration of the penetrant cannot be depleted [113]. Infinite dose experiments are beneficial for determining a compound's ability to penetrate the skin. Conversely, finite dose experiments are more representative of occupational exposures and can predict maximal absorption rate per exposure and total absorption per exposure. However, the concentration of the penetrant in the dosing vehicle can change as it is absorbed into the skin, or if the dosing vehicle is absorbed or evaporates, which can be difficult to predict for firefighter exposure. Figure 19 depicts the differences between infinite dose and finite dose flux. The top image of Figure 19 an infinite dose shows an increase in cumulative absorption as time goes on compared to the finite dose that levels out as the entire dose is absorbed. Inversely, the bottom image of Figure 19 shows the difference in concentration between the infinite and finite doses across time. The infinite dose is maintained constant while the finite dose decreases as it is absorbed into the skin.

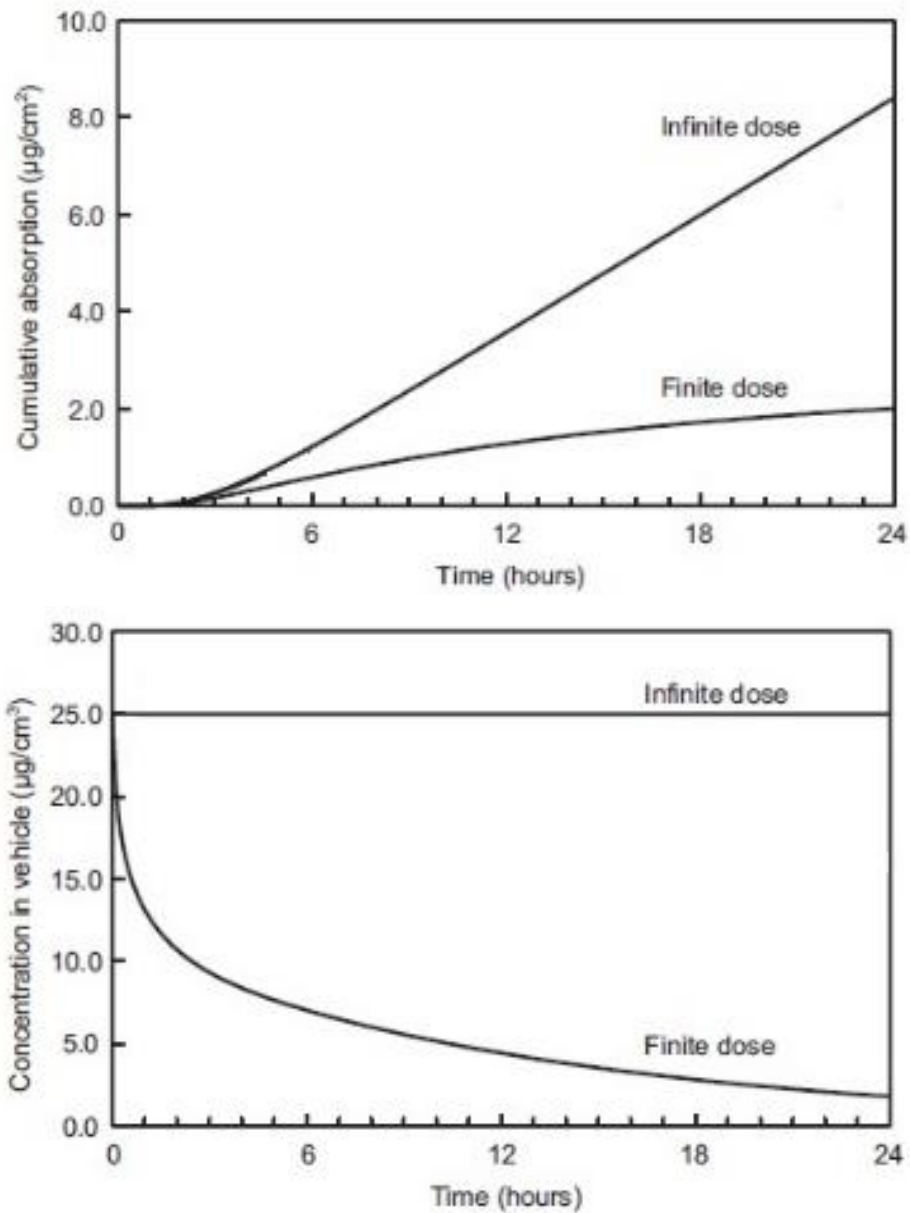


Figure 19: Concentrations of the penetrating chemical in Infinite and Finite Dose Experiments [94]. (Top) Concentration of the penetrant into the skin and described as cumulative absorption ($\mu\text{g}/\text{cm}^2$) (Bottom) Concentration of the penetrant in the dosing vehicle [114]

2.7.3. Factors of Dermal Absorption

The theory and mechanism of dermal absorption is rather straightforward. Simply put, a chemical that encounters the skin has to diffuse through the skin's defensive barrier to penetrate deep enough to be absorbed into the body. However, there are numerous skin-specific, environmental, and physico-chemical factors to consider when determining the dermal absorption of a chemical penetrant. These factors then become difficult to keep track of during occupational exposure studies. Highlighting the need and benefits of estimating potential exposures through controlled laboratory experiments.

2.7.3.1. Skin Factors

The skin acts as the barrier against all chemical penetrants. Possibly the most important factor regarding the penetrative resistance is skin thickness, which varies across different anatomical sites. The thickness of the stratum corneum can range from 5 μm in the scrotum in men to 15 μm in the abdomen, a commonly used area for percutaneous absorption studies, and up to 400 and 600 μm thick in the palm and soles of the hands and feet, respectively [120]. Chilcot and coworkers demonstrated the differences of dermal absorption in various anatomical regions using the nerve agent VX (a lipophilic organophosphate compound), shown in Figure 20, and showed that the thinnest skin had the greatest permeability [114]. Furthermore, additional studies have demonstrated that skin permeability is influenced by the anatomical region [121, 122]. In the case of firefighter skin contamination, the neck, hands, calf, and upper leg area were found to be most susceptible to particulate deposition, some of which are higher risk of chemical penetration [49]. Cross contamination is also a problem that fire responders must be cognizant of during post-fire activities and while departing from the scene. The effect of anatomical variation in dermal absorption has been found across several animal species (rats, mice, pigs, and monkeys) using a wide variety of chemicals (PAHs, pesticides, steroids, and others) [113, 114, 121, 122, 123].

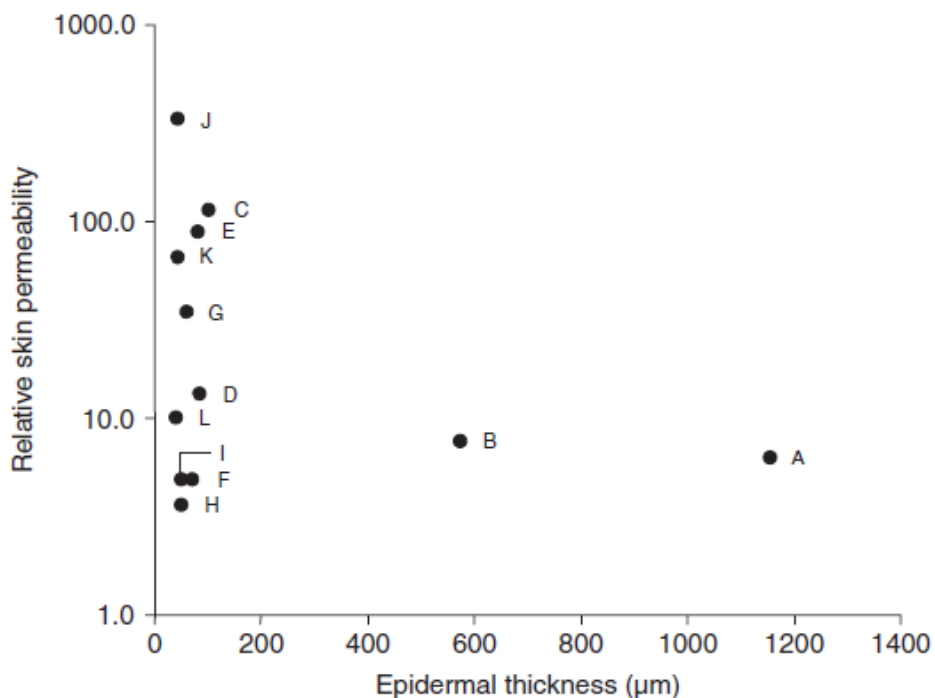


Figure 20: Skin permeability as a function of skin thickness measured in human volunteers to nerve agent VX (0-ethyl-S-[diisopropylamino)ethyl] methylphosphonothioate). Anatomical regions in order of thickest to thinnest: A = plantar; B = palmar; C = cheek; D = nape of neck; E = forehead; F = back; G = groin; H = underside of the forearm; I = topside of the forearm; J = scrotum; K = armpit; L = abdomen [114].

As mentioned previously, the primary function of the skin is to serve as a barrier against the environment, which also means that the skin is the most susceptible to damage through cuts, abrasions, disease, or ultra-violet radiation. Damaged skin does not provide the same level of resistance against xenobiotics and chemicals. Few studies have measured percutaneous absorption through damaged human skin but those that demonstrate a modest but clear enhancement in absorption favor hydrophilic molecules [124]. Generally, UV exposure benefits human health by mediation between the natural synthesis of vitamin D and endorphins in the skin, however, exposure should be monitored because acute exposure can cause damage and UV radiation is classified as a complete carcinogen [125]. One of the most easily recognizable causes of acute UV exposure is sunburn, caused by a cascade of cytokines, vasoactive and neuroactive mediators in the skin creating an inflammatory response. Cell damage occurs when the melanin and eumelanin compounds in the skin are overwhelmed by UV photons and as a result keratinocytes die. Hung et al. (2015) exposed skin to UVB and found an increase in transepidermal water loss, meaning that the SC integrity was disrupted, leading to an increase in

skin permeation and two-fold increase in skin absorption of tretinoin, a derivative of vitamin A [126]. Additional studies have investigated the penetration of nanoparticles in damaged skin through needle-abrasion and found that damaged skin had higher concentrations of the penetrant nanoparticle [127, 128].

In the fire service industry, there is a popular belief, “that for every degree increase in skin temperature results in a 400% increase in dermal absorption occurs.” Identifying the source of this claim has been extremely difficult and after identifying the source the person who originally said this has backed away from the claim. Temperature can play a role in dermal absorption; however, it is unlikely to be to the extent that this adage states. However, there have been several pharmacological studies on the effect that increased skin and donor solution temperature has on chemical absorption and skin permeability. Jetzer et al. (1998) exposed the SC to aqueous solutions ranging from 10 – 37°C and found that the K_p varied 3 – 7× as a function of dosing solution temperature [129, 130]. Durrheim et al. (1980) also showed that percutaneous absorption rates vary over a range of 29 – 37°C of the dosing solution temperature [131]. Trabaris et al. (2012) also showed that the dermal flux of haloacetonitriles and chloral hydrate increased by 50 – 170% with an increase of dosing solution temperature across a range of 25 – 40°C [123]. Tominaga et al. (2010) findings agree with previous research that, donor solution temperature increases chemical permeation across the skin [132]. While many studies looked at the effect of the dosing solution temperature, Kilo et al. (2020) investigated the effect of skin temperature on dermal absorption. The absorption of lipophilic and hydrophilic compounds both demonstrated temperature dependent variations in penetration behavior, including cumulative absorption and transdermal absorption, over a range of 25 – 39°C [133]. The differences in absorption were greatest within 45 minutes after exposure.

There are a few theories on how temperature of the skin will change the rate of chemical penetration and absorption. One theory is that as skin temperature increases the rate of penetration increases by changing the structure of the stratum corneum and the behavior of the lipid matrix [120, 134, 135]. The second theory is that as skin temperature increases the body temperature must also increase, leading to physiological responses such as increased blood flow and sweating. When the blood flow in the skin is increased the rate of chemical removal from the skin and into the body is also increased. However, this mainly affects the amount of lipophilic chemicals absorbed, as their clearance by blood is often rate limiting [113, 136]. Ultimately,

temperature may be more important than other factors during short-term exposures such as firefighting.

2.7.3.2. Chemical Factors

In addition to the skin and its properties that influence its barrier effectiveness, the physical and physicochemical properties of a penetrating chemical can also determine its ability to permeate human skin. The molecular weight and structure, octanol-water partition coefficient, ionization state, concentration or dose, dosing vehicle whether a liquid, cream, particulate, or other, can drastically change a chemical's ability to be absorbed into the body.

Lipophilic compounds are more likely than hydrophilic compounds to penetrate the skin as they easily penetrate the lipid bilayers and cell membranes of the corneocytes comprising the skin. Lipophilic compounds can easily navigate lipids situated between the corneocytes but struggle to penetrate the hydrophilic layers of the dermis. Conversely, hydrophilic compounds quickly pass through the hydrophilic layers of skin but struggle to penetrate the lipophilic stratum corneum of the skin, reinforcing why the brick-and-mortar structure provides excellent protection against a range of penetrants.

The size of the penetrating chemical can limit its ability to penetrate the skin. Bos and Meindardi (2001) proposed that compounds with a molecular weight less than 500 Dalton can easily pass through the stratum corneum, but as compounds increase in molecular weight above 500 Dalton their absorption rapidly declines. The 500 Dalton Rule is based on three primary arguments: 1) virtually all compounds that cause allergic reactions of the skin are under 500 Dalton, whereas large molecules are not known to cause these allergic reactions; 2) the most commonly used active ingredients used in dermal treatments, such as creams and lotions, are all under 500 Dalton; and 3) all known topical drugs used in transdermal drug-delivery systems are under 500 Dalton [137]. Regarding PAH exposure, the largest PAH of the 16 priority compounds is 276 Dalton, meaning all PAHS could be absorbed through the skin.

The octanol-water coefficient, defined as K_{ow} or $\log K_{ow}$ or $\log P$, can be used to quickly predict whether a chemical will penetrate the skin. Several researchers have attempted to demonstrate a correlation between percutaneous absorption and partitioning behavior. There is a general tendency that as lipophilicity increases (increasing $\log K_{ow}$), the permeability coefficient K_p increases, but there are some exceptions to the trend, for example phenols. The difficulty in definitively establishing a relationship between $\log K_{ow}$ and absorption stems from the fact that

there are several water-immiscible phases that can be used to determine $\log K_{ow}$, such as n-hexane, dichloromethane, chloroform, or silicone rubber. This means using $\log K_{ow}$ can be applicable to some chemical classes while not reflecting the lipophilicity of other chemical classes. Korinth et al. (2012) examined the potential of using $\log P$ to predict dermal penetration behavior of amphiphilic compounds in aqueous solutions and found a consistent relationship between the percutaneous penetration behavior and $\log P$ for 13/15 tested compounds [138]. Several mathematic models have been generated to predict skin permeation using two or more chemical properties, the most popular two properties being molecular weight and octanol-water partition coefficient. In 1995, one study worked to evaluate five current skin permeation models and discovered that only one model, the Robinson model (shown in Equation 10), could be recommended for predicting the skin permeation coefficient [139]. There have been several more mathematical models aiming to predict skin absorption but there has yet to be a model to replace experimentation data. As a result, the octanol-water partition coefficient should only be used as a method to approximate dermal exposure for risk assessments or predict a chemicals ability to penetrate the skin.

Equation 10: Robinson (Revised) Skin Permeation Model

$$K_p = \frac{1}{\frac{1}{K_{psc} + K_{pol}} + \frac{1}{K_{aq}}}$$

Equation 11: Permeation Coefficient of Lipid Fraction of Stratum Corneum

$$\log K_{psc} = b1 + b2 * \log K_{ow} + b3 * MW^{0.5}$$

Equation 12: Permeation Coefficient of the Protein Fraction of Stratum Corneum

$$K_{pol} = \frac{b4}{\sqrt{MW}}$$

Equation 13: Permeation Coefficient of Watery Dermis Layer

$$K_{aq} = \frac{b5}{\sqrt{MW}}$$

Another property that influences a chemical's ability to penetrate the skin is whether the penetrating chemical is charged. Ionized chemical species have a challenging time penetrating the skin. The presence of proteins gives the SC both positive and negative charge groups. However, there is a greater presence of negatively charged groups resulting in a net negative charge [114]. Hence, positively charged ions are more likely to penetrate the SC than negatively charged ions but are still less likely than neutral compounds. Neutral compounds are the most likely to penetrate the skin because dermal absorption is a passive process meaning there is no energy that will help transport charged species across the SC barrier. Comparative studies between ionized chemical species and their non-ionized counterparts found that the permeability coefficient for non-ionized compounds is frequently one to two orders of magnitude larger than the ionized forms of the chemical [140]. The difference in dermal penetration between ionized and non-ionized chemicals is greater for lipophilic species than hydrophilic species [113]. In dermal absorption studies, the dosing vehicle should be chosen carefully to favor the non-ionized form of the chemical species.

As just stated, the importance of the dosing vehicle should not be overlooked. In pharmaceutical applications the goal of the dosing vehicle is to provide the maximum amount of transfer of chemical from the vehicle to the skin. Dosing vehicles with comparable properties to the penetrating chemical, for example a lipophilic dosing vehicle and a lipophilic compound, can reduce the dermal absorption of the penetrating chemical because there can be a similar or higher affinity for the vehicle and subsequently the chemical will not partition into the skin. In the case of firefighters and fire investigators the most common vehicle is particulate matter, smoke, and soot. Studies that have used soil, sediment, or particulates as the dosing vehicle have all shown that skin penetration is less than pure or liquid chemicals [102].

Wester and coworkers compared the effects of dosing vehicles on percutaneous absorption of benzo[a]pyrene using an acetone solution and soil *in vitro* using a flow-through diffusion cell [103]. Benzo[a]pyrene readily penetrated human cadaver skin in the acetone vehicle compared to the soil vehicle, which had significantly less benzo[a]pyrene penetrate the skin. When benzo[a]pyrene was applied to rhesus monkey skin the average absorption with acetone was $51 \pm 22\%$ compared to $13.2 \pm 4\%$ average absorption with a soil vehicle [103]. Acetone is known to damage the skin cells, thus reducing the effectiveness of the skin barrier, and leading to increased absorption [141]. A similar study by Yang and coworkers compared the

dosing vehicle effects on percutaneous absorption of benzo[a]pyrene using rats [142]. An aqueous dose of benzo[a]pyrene applied to the skin absorbed four to five times more than that of the soil vehicle. The low absorption of benzo[a]pyrene in the soil vehicle was due to the reduced concentration of the compound that contacted the skin, indicating that strong soil binding of PAHs reduces dermal absorption. An earlier study by Yang and coworkers investigated the percutaneous absorption of benzo[a]pyrene *in vivo* and *in vitro* using rats [104]. *In vitro* results showed that 2.1% of the dose (9-10 $\mu\text{g}/\text{cm}^2$) diffused into the receptor fluid over five days. The liquid dose vehicles resulted in greater absorption through the skin compared to the soil vehicles, which had significantly less absorption.

2.7.4. Methods and Techniques to Study Dermal Absorption

In vivo studies are the gold standard to determine chemical absorption, however, it is difficult to obtain human or animal skin due to ethical concerns and strict regulations. *In vitro* absorption studies are used more frequently because they are more economical, minimize or eliminate the use of animals, and directly measure test compounds absorbed into and through the skin [143]. Furthermore, both of these methods will obtain the same dermal absorption values such as permeability coefficient, partition coefficient, and diffusion coefficient, which are critical for values that are used to predict the dermal absorption of a chemical [144, 145, 146]. The type of diffusion system is selected out of convenience, cost, availability, or relevance. Diffusion cells, either Franz or Flow-Through, are popular *in vitro* methods, where a newer test method called, parallel artificial membrane permeability assay (PAMPA), has been gaining acceptance in the pharmaceutical industry because of its high throughput screening applications, but remains a recent technology with much needed research and testing. Human, animal, and synthetic skin models have been used to assess the permeation of drugs, lotions and cremes, and chemicals of toxicological interest. The permeation values of a chemical in animal and synthetic models can be compared against human skin and determined the model's ability to predict human skin absorption.

2.7.4.1. Static Diffusion Cell Experiments

In the Franz or flow-through diffusion cell experiment a test chemical is dosed on the surface of the test skin or membrane. Perfusate samples are collected throughout the experiment. The degree of absorption and depth of penetration is determined at the end of the experiment [147]. Sometimes the skin or membrane can behave like a reservoir for the test chemical. To

accurately determine systematic skin absorption in this case, both skin and receptor fluid should be measured for the test chemical. When working with volatile compounds, the recovery of the test compounds can be lower than non-volatile compounds, which should have recoveries of at least 90% [148].

The static diffusion cell systems are simpler in design compared to the flow-through diffusion cell system and are based on the Franz diffusion cell. An illustration of a typical set up of a static diffusion cell experiment is shown in Figure 21. The skin or membrane sits atop the receptor chamber and is open to the environment. The donor chamber is applied to the top of the skin or membrane to apply the test compounds. The receptor fluid is collected in a chamber below the skin or membrane and is continuously stirred with a magnetic stir bar. Periodically aliquots of the receptor fluid are collected through a side arm for analysis. The static diffusion cell experiment remains relevant because of its relatively low cost and customizability to change the size of the opening, which can allow studies with transdermal devices [148].

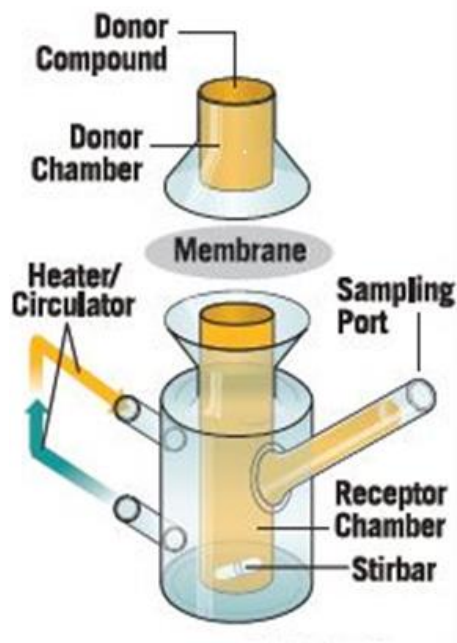


Figure 21: Illustration of a Static One-Chambered Diffusion Cell

2.7.4.2. Flow-Through Diffusion Cell Experiments

The flow-through diffusion cell is a more complex system than the static diffusion cell system. There are three major components in the flow-through cell diffusion test: the heating blocks, peristaltic pump and tubing, and the sample collecting apparatus. The heating blocks are to keep the skin or membrane samples at a set temperature often like the human body. The peristaltic pump and tubing pump the dissolved chemical onto the surface of the skin samples. The receptor fluids can be a saline solution or other solvent systems, but formulations should aim to represent in vivo systems. The artificial medium in the sampling apparatus may vary but should be physiochemically similar to blood to best mimic oncotic pressure in vivo [147]. A typical set up of a flow-through diffusion cell experiment can be seen in the illustration found in Figure 22. These experiments typically run from 8-12 hours to simulate worker exposure but can run for 24 hours [147, 148]. Flow-through diffusion cell experiments are better suited to evaluate dermal absorption than static diffusion cell systems because they better mimic environmental conditions while not excessively hydrating the skin [147].

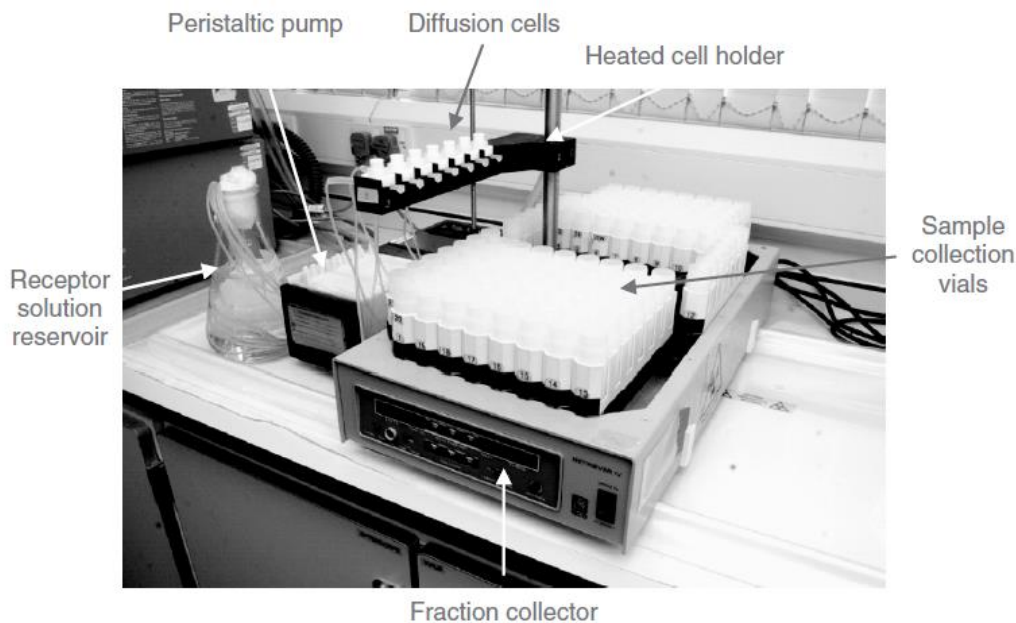


Figure 22: Illustration of the flow-through diffusion cell system in an environmentally controlled chamber [114]

2.7.4.3. Parallel Artificial Membrane Permeability Assays

The PAMPA is a recent development first introduced by Kansy in 1998 to investigate the passive absorption processes and has since been adapted to classify molecules at the earliest stages of drug discovery in the pharmaceutical industry [149]. PAMPA models have been published for the prediction of gastrointestinal absorption, modeling the blood brain barrier, and skin penetration [149]. For skin-PAMPA models the goal is to match the permeability of the rate-limiting barrier in human skin by using synthetic certramides, which are analogs to the ceramides present in the stratum corneum, and a similar lipid mixture of certramide, free fatty acid, and cholesterol.

The PAMPA system uses two aqueous buffer solution wells separated by an artificial membrane, supported by a porous hydrophobic filter plate matrix, shown in **Error! Reference source not found.**. During the experiment, the test compound is diluted in buffer and placed in the donor well and passes through the artificial membrane into the acceptor well via passive diffusion [150]. The rate of permeation can be determined by the compounds effective permeability [151]

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Although the PAMPA system is much newer relative to the diffusion cell systems it does have some distinct advantages. The first advantage is the significant increase in testing volume and throughput. The PAMPA system can use a 96 well plate whereas the traditional diffusion cells can reliably run only a handful of cells simultaneously. This increases time effectiveness while reducing costs [150]. The system also has a higher tolerance to a wider pH range and higher dimethyl sulfoxide content [152]. Even though the PAMPA system is relatively new and needs further investigation, it has already been established as a quick and cost-effective research tool that can serve as a useful model of skin penetration in pharmaceutical and cosmetic research [149, 150]. While there are notable advantages to the new testing system some disadvantages remain. Research has been limited to pharmaceutical, drug discovery, and cosmetic research. As a result, there is not a predefined membrane that should be selected for testing the skin penetration of environmental contaminants such as polycyclic aromatic hydrocarbons. For these reasons the PAMPA system is not ideal for the skin penetration tests of fireground contaminants.

2.7.5. Human Skin Surrogates

Human skin is the gold standard for collecting data on chemical, drug, or xenobiotic penetration. However, human subject tests using potentially harmful or carcinogenic chemicals is unethical. This is one of the primary reasons why *in vitro* tests are so popular. Human cadaver skin or excess skin from surgical procedures can be used in these types of tests and are the best alternatives to human subject testing, but sourcing human skin from these means is difficult and supply is limited. To reduce the dependency on human skin, significant research has been done to identify an animal or synthetic skin model that can be used as a human skin surrogate.

2.7.5.1. Animal Skin Models

When using animals for dermal absorption studies, there are clear differences in hair or fur density. An animals' fur/hair changes their skin's morphology and function while also providing extra protection from their environment [153]. To prevent the effect of fur/hair on dermal absorption, animal subjects are shaved, and the skin is washed and cleaned [148]. Next, the animal skin is cut using a dermatome to a thickness similar to that of human skin, about 200-300 μm [143].

Several species of animals ranging from rats, mice, and other rodents, to rabbits, monkeys, snakeskin, and pigs have been tested in dermatotoxicological studies. While no single animal species has the exact same morphology and physiology of human skin, some species are

used more than others. The most used animal skin model is rodent skin, because of its availability and low cost make it a popular choice for preliminary stages of testing or experiments. Compared to human skin, rodent skin is more permeable and often overestimates dermal absorption because their skin cells are arranged in columns, unlike the “brick and mortar” structure of human skin, providing a more direct route to the underlying skin layers [114]. Rodent skin has been found to be 40 to 1600 times more permeable than human skin and found to have the most significant differences relative to other animal skin models when compared back to human skin [153, 154]. These wide ranging differences in absorption result from the differences in skin morphology, where the skin cells in rodent skin are stacked on top of each other rather than offset as in pig and human skin. Rodent skin models make for a better preliminary assessment of dermal absorption of drugs and chemicals than a model for human skin after been repeatedly found to be orders of magnitude different to human skin [153].

Although no animal skin model can replicate the absorption in human skin, pig or porcine skin is the most relevant animal model and has been reviewed and validated over many years [114, 155]. Porcine skin is most analogous to human skin because of its similar stratum corneum structure and skin morphology to human skin. For most compounds tested, pig skin was comparable to human skin absorption ranging 50 – 150% [153, 155].

2.7.5.2. Synthetic Skin Models

Although there have been mass amounts of research done on animals, animal right groups continue to push for the elimination of animal testing. The United Kingdom is among the strictest in the world, with the Animals Scientific Procedures Act 1986 requiring that experiments must be regulated by individuals with approved licenses and procedures should involve the minimum number animals needed to produce statistically valid results [114]. Although the UK is one of the strictest, there are countries with no formal requirements regarding the use of animals for research. To ensure that quality data can still be gathered without using human or animal skin the focus of skin model research has shifted towards synthetic skin models. Synthetic skin models could be more advantageous than animal skin models because of their low cost, ease of storage, and better control over physical properties. Because of these characteristics, synthetic skin models avoid the controversy associated with animal testing and can have better reproducibility and reliability. Several synthetic materials have been used to model the sweating, surface, mechanical, acoustic, optical, and thermal

properties of human skin [156]. Figure 23 shows the various model types used to simulate specific properties of human skin. These models include liquid suspensions, gelatinous substances, elastomers, epoxy resin and textiles.

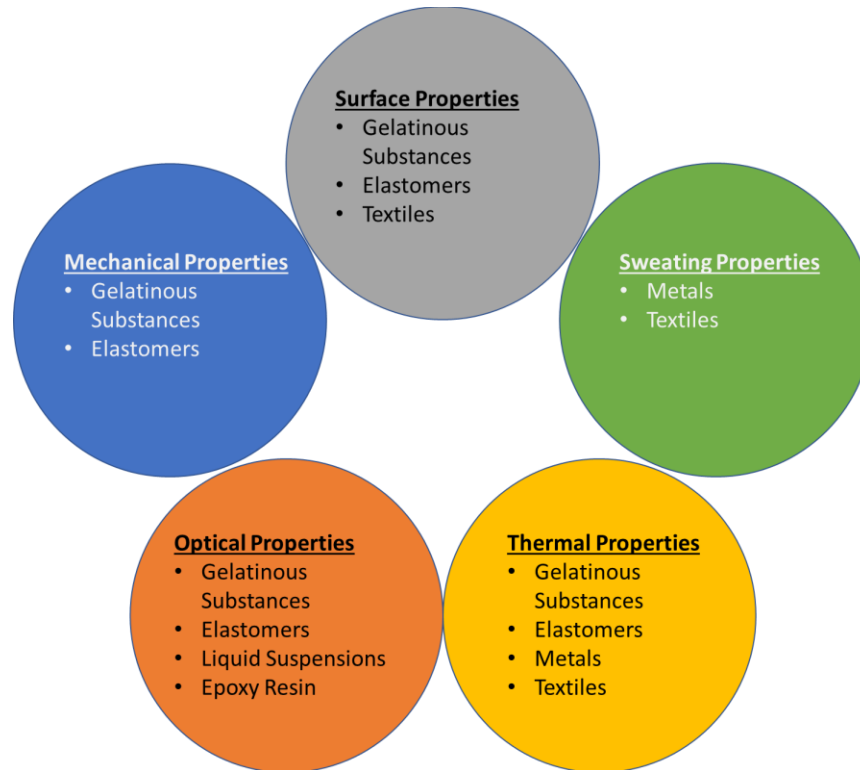


Figure 23: Synthetic materials used to simulate various properties of human skin [144]

A study by Uchida and coworkers (2016) evaluated a silicone membrane as an alternative to human skin for determining skin permeation parameters of chemical compounds [157]. The permeability coefficients were calculated for silicone membranes and compared to human and hairless rat skin. The tested silicone membrane produced similar permeation coefficients for hydrophilic compounds, whereas the permeation coefficient of amphiphilic compounds was 10× higher in silicone membrane than human and hairless rat skin. Furthermore, the permeation coefficient of lipophilic compounds was 100 times higher in the silicone membrane than human and hairless rat skin. Even though the silicone membrane was not similar to human or hairless rat skin, there was a significant correlation observed between the partition coefficient values in human skin and silicone ($r=0.869$) and in hairless rat skin and silicone ($r=0.823$) [157].

Strat-M® is a synthetic membrane model for transdermal diffusion intended to predict the diffusion of test compounds in human skin. It has been used as a screening tool for active pharmaceutical ingredients, cosmetics, formulations, personal care products, pesticides, and chemicals [158]. The Strat-M® membrane is a multilayered structure with a tight top layer to resemble the stratum corneum, two layers of polyethersulfone to resemble the dermis of human skin, and polyolefin non-woven fabric support to resemble the subcutaneous tissue in human skin, seen in Figure 24. Uchida and coworkers (2015) showed a strong correlation between log P values for Strat-M® membrane and hairless rat skin ($r=0.970$) and for Strat-M® membrane and human skin ($r=0.929$). Additionally, the more lipophilic compounds had higher partition coefficient values through each membrane tested. This study shows that the Strat-M® membrane can be used to predict those for human and rat skin, especially for chemical compounds with molecular weights between 151 and 288 and log K_{ow} between -0.90 and 3.53 [144]. Furthermore, the effects of penetration enhancers have been evaluated in the Strat-M® membrane and compared to human cadaver skin [159]. Although the Strat-M® membrane was more permeable the enhancement factor for all five test formulations were similar for the Strat-M® membrane and human skin. The flux between the Strat-M® membrane and human cadaver skin was high with a correlation valuation of 0.99 further showing the Strat-M® membrane's usefulness for predicting chemical penetration in human skin. [159].

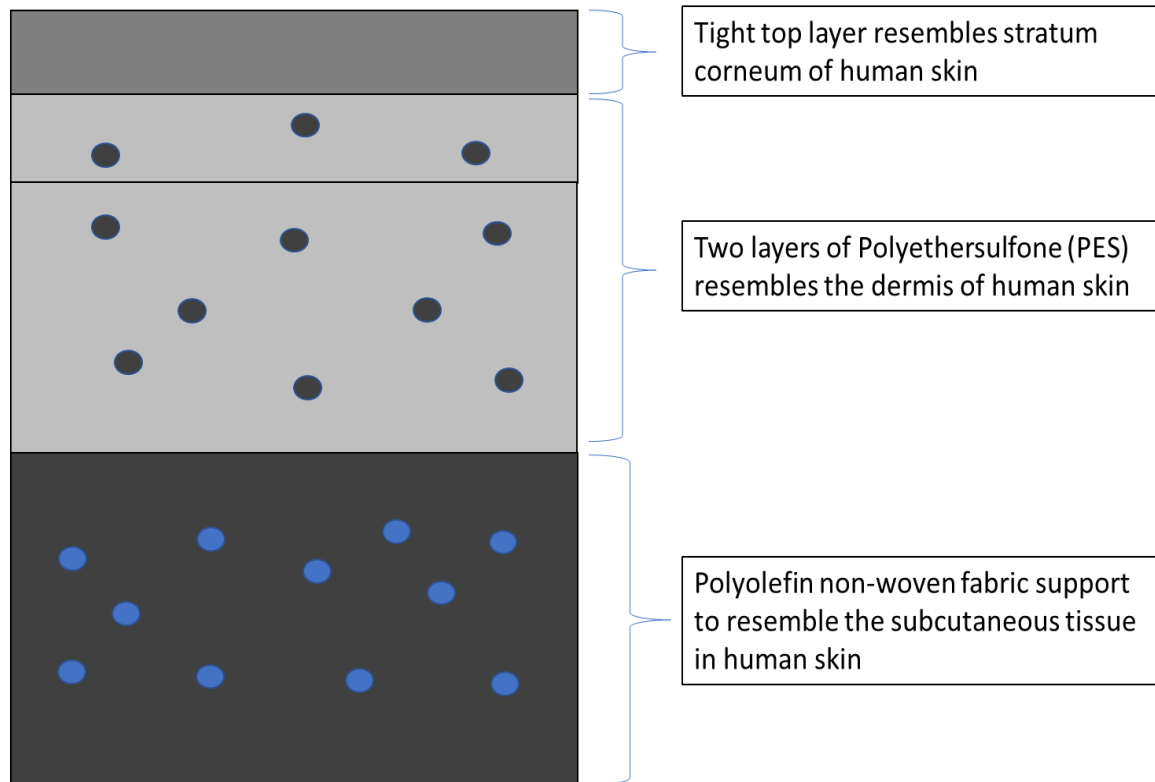


Figure 24: Illustration of the multilayered structure of Strat-M® membrane [160]

SynDaver™ is a company that manufactures sophisticated synthetic models of the entire human body or specific body parts such as muscles, tendons, veins, arteries, organs, and skin. SynDaver™ tissue plates have been used for training intradermal injections and skin surgery procedures by medical professionals. Although the specific ingredients are proprietary, information gathered from their website states that the product is made from a polymer, likely polyurethane, water, and salt. Polyurethanes are polymers that can easily change their properties by changing the ratio of monomers and additives, making them a likely primary component of the SynDaver tissue plate.

There are few studies that have compared the permeation between SynDaver™ tissue plates and human skin, but mechanical and deformation behavior comparisons have been made [161]. SynDaver™ tissue plates were found to undergo less deformation under equivalent loads compared to human skin and decreased in friction under wet conditions compared to human skin. The permeation of SynDaver™ tissue plates has yet to be tested but its layered structure and similar physical properties, such as resistive force exertion, make it a candidate for human skin surrogate selection.

2.8. Fireground Decontamination Wipes

2.8.1. Decontamination Wipes

To mitigate fire responder chemical exposures through dermal absorption new, on-scene decontamination (decon) procedures are being developed and implemented. These strategies range from bagging up contaminated equipment for transport back to the fire station to where it can be cleaned, brushing down firefighters who entered the burning structure using air, dry brushing, or a wet brush with soap, and showering upon immediately returning to the fire station. Each strategy has advantages and disadvantages, as well as range in their effectiveness for removing fireground contaminants from the skin. However, humans can be stubborn and resistant to adopting new policies and research has shown that firefighters less likely to follow decontamination strategies that are time consuming and labor intensive [71]. Therefore, to make it easier for fire responders to follow some sort of decontamination procedure at the scene, decontamination wipes have been heavily marketed towards firefighters and first responders as both an effective and convenient decontamination tool.

Fire responders can be limited in their selection of on-scene decontamination procedures due to the regional variations in climate. Taking the three different decontamination strategies used in the Fent et al. (2017) paper as an example, fire responders in the frigid Northern parts of the United States would be less inclined to implement a wet-soap brushing method for risk of individuals experiencing hypothermia and overall comfort, whereas those in warmer southern climates would not have low temperature barriers for implementation. The purpose of decontamination wipes is to serve as a tool in a simple decontamination method that every fire responder can quickly and easily perform before returning home or to the fire station.

Even though the use decontamination wipes is well intentioned, there has been an abundance of different products ranging from wipes similar to baby wipes, towelettes, and towels. None of these have been tested using a standardized test method or certified testing agency for their safety or effectiveness at removing contaminants from the skin. With the recent mass introduction of decontamination wipes and the lack of data on their safety and effectiveness firefighters are likely left with more questions than answers.

2.8.2. Wipe Sampling

Wiping a surface has been shown to be one of the most effective methods to physically remove contaminants from a surface [162]. Wipe sampling methods hold several advantages

over other surface contamination removal methods, because of the physical characteristics, size, shape, and surface topography of the wipes used in these methods. However, surface contaminants are not restricted to pure chemicals. Other contaminants may include particulate matter, microorganisms, and fibers, seen in Figure 25. Wipe sampling has been adapted to assess dermal exposure or surface contamination of pesticides [163], flame retardants [164, 165], trace explosives and chemical warfare agents [166], bisphenol-A (BPA) [167], perfluoroalkyl substances (PFASs) [168], PAHs in health care workers [169], automotive repair technicians [170], and road paving workers [171, 172]. As mentioned in the previous section, wipe sampling has been utilized in previous studies for analyzing surface contamination of turnout gear and skin of firefighters [47, 48, 53, 173, 174]. It is well known that PAHs adsorb onto particulate matter (PM) produced during a fire [175, 176]. To determine surface contamination of PAHs, wipe sampling methods have been used to remove particle-bound-PAHs from turnout gear or human skin.

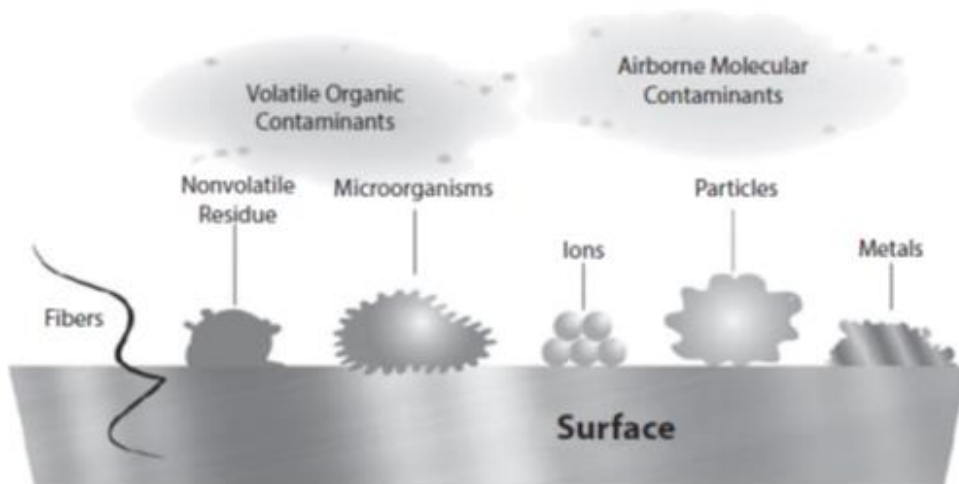


Figure 25: Examples of Different Types of Surface Contaminants [162]

2.8.2.1. Variables in Wipe Sampling

Even though wipe sampling is used across several fields of research the methods used are rarely consistent. There are several variables that can increase or decrease the recovery of an analyte from a surface during wipe sampling. For example, the variables within the wipe itself, the contaminated surface, solvents, or additives used, and the sampling method can change

analyte collection efficiency. Furthermore, the interaction between the wipe and substrate surface needs to be considered to determine the best wipe and method to maximize contaminant removal.

Wipe variables that influence collection efficiency include the fiber, wipe construction, and solvents used in the wipe [170]. Figure 26 illustrates the microscopic surface topography of a wipe. Fibers used in clothing, and other textile products can be natural (cellulose, cotton, animal fiber, silk, hemp) or man-made (nylon, Nomex, or polyester) all of which can be used to create wipes. Polyester is a popular fiber used in health care wipes because of its inherent cleanliness [170].

The surface area of the wipe available for contaminant collection is a large factor that determines collection efficiency and differs across brands of wipes. Wipes intended for cleaning skin often contain solvents and other additives such as moisturizers and fragrances; these too will impact the wipes ability to remove contaminants and particles from a surface.

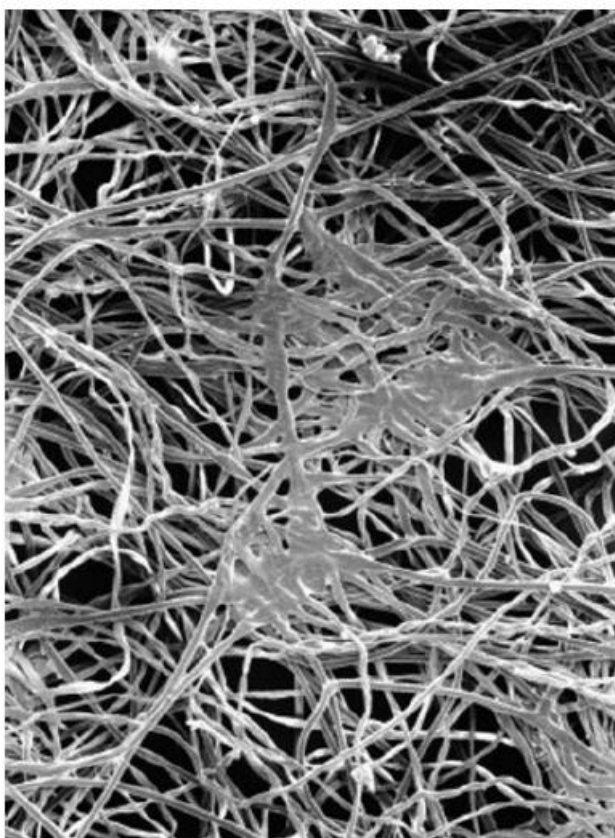


Figure 26: Scanning Electron Microscope image of a hydro-entangled nonwoven demonstrating the fiber pattern of the construction [162]

The substrate surface plays a pivotal role in wipe sampling. Although human skin is not entirely a porous surface, the layered complex system of skin cells behaves like a porous surface. Collection efficiencies of contaminants from porous surfaces have been reported to be drastically lower than their non-porous counterparts [177]. Unlike nonporous surfaces which are flat and consistent, porous surfaces have cavities or holes that entrap particles, making it difficult for a wipe to reach and remove particles from the surface. This phenomenon can be exemplified by a wipe sampling study where 90 μm particles were imbedded into the topographical valleys of a nylon zipper seen by a microscope [166].

Sampling methods for wipes are rarely the same because the analyte or compound of interest may have different physicochemical properties that require changes in the method to produce acceptable results. During method development, if recovery using a single wipe is low then multiple sampling passes with the sample wipe can be used to increase recovery and reduce variability.

When assessing the extent of contamination on humans, it is important to keep the size of the sampling area consistent and is regularly done with a template. When considering organic compounds such as PAHs, solvents or additives can increase collection efficiency. However, these solvents or additives must be chosen carefully because they can be destructive to the substrate surface, or harmful to human subjects. Solvents that easily solubilize PAHs like dichloromethane, hexane, methanol, and acetone are known to be harmful to humans and excessive skin contact can cause nerve damage, irritation, burns or blindness. Safer substances such as corn oil, sunflower oil, or other lipophilic substances have been applied to the surface, often human skin, prior to wiping to increase the mobility of the PAHs [48, 171, 172].

2.8.2.2. Wipe Sampling Mechanisms for Removing Particles from Substrates

Particulates can be found on nearly all pieces of turnout gear as well as the skin after a firefighter exits a burning structure. Particles are held in place on a substrate surface via adhesion forces, van der Waals, electrostatic forces, or capillary forces acting at the interface between the particle and the substrate surface [162]. Van der Waals forces come from changing electron densities of molecules creating an attractive electromagnetic force. These forces tend to be weak, spanning across nanometer distances. However, as the number of interactions increases the magnitude of this interaction increases. Up to distances of 20 μm , the controlling forces in particle adhesion may be electrostatic forces depending on the properties of the particles,

surfaces, and intervening medium. In dry environments, like those inside a burning structure, electrostatic forces are controlled by the charge and potential, conductivity, and separation distance of the particle and surface. Capillary forces are highly dependent on the relative humidity of the environment. Water molecules in humid air minimize their free energy by absorbing onto surfaces at low humidity and condensing onto surfaces at higher humidity [162]. The capillary forces are a function of the particle radius and the surface tension of the liquid. Aside from the adhesive forces that hold particles, the surface topography can also hold a particle on a substrate. In addition to the adhesion forces, physical entrapment of particles in the gaps and valleys of a garment can keep particles on the surface or within fire responder personal protective equipment.

To remove particles containing PAHs from firefighter turnout gear or skin, the forces of attraction between the particle and substrate surface must be overcome. At a microscopic level all wipes can be reduced to a series of fibers or polymer filaments which into contact the surface of interest. When in contact with a surface, the fibers of a wipe interact with the particles either through rolling, lifting, or sliding the particles off the substrate surface. The fibers can also entangle particles in between fibers preventing redeposition of the particle on the surface, as illustrated in Figure 27 [166, 178]. Sliding is not as common as rolling or lifting mechanisms because the force required for sliding is generally greater than that needed for rolling. Additionally, particles can be removed from a substrate surface by electrostatic attraction. If a large enough difference between the wipe and surface occurs particles may “jump” across the interaction gap. However, this mechanism is minimal as it contributes at the micrometer scale and is ineffective if the substrate surface has moisture [166, 179].

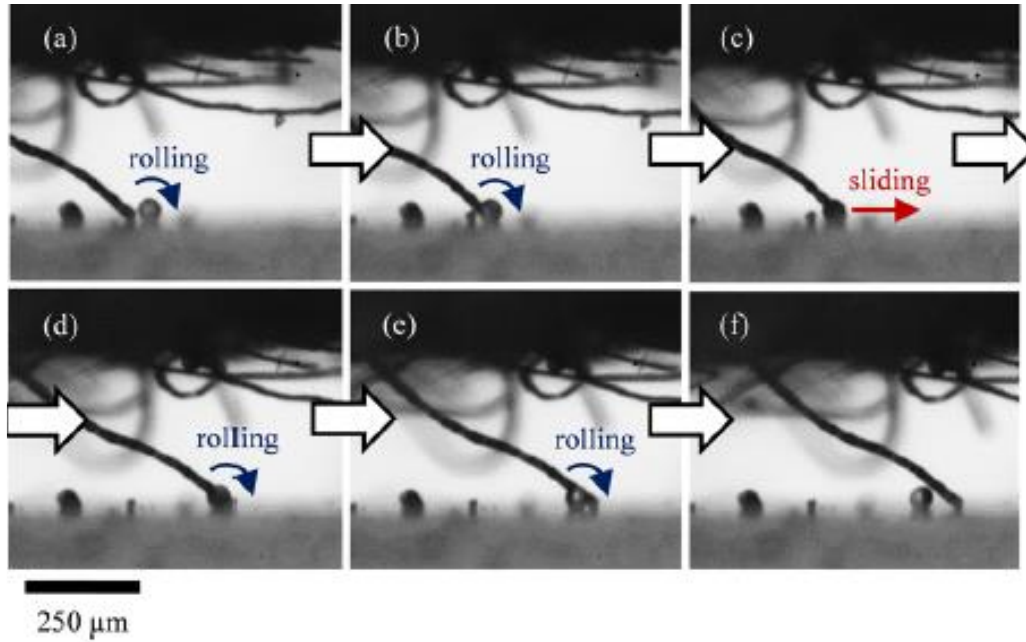


Figure 27: Sequence of images, showing particle rolling motions occurring in frames a-f, and sliding motions in c-d, resulting from interactions between an individual Nomex wipe fiber and a 50 μ m diameter polyethylene Janus particle on a glass substrate [166]

2.8.2.3. Wipe Sampling Studies

Materials currently being sampled by wiping with cloth or swabs include explosives, illicit drugs, nuclear particles, biological pathogens, pesticides, environmental contaminants, dusts, heavy metals, pesticides, and pharmaceutical residues [180]. Collection efficiencies from wipe-sampling are dependent on particle size, shape, and adhesion to the surface.

One of the earliest studies to investigate the differences in recovery based on washing solution was a comparative study by Wester and coworkers that examined the removal of [¹⁴C]-Methylenebis(phenyl-isocyanate) (MDI) from the skin of rhesus monkey using lipophilic solutions (polypropylene glycol, polyglycol-based cleanser and corn oil) versus aqueous (0%, 5%, or 50% soap with water) washing solutions, seen in Table 8 [181]. The aqueous solutions had 60-70% removal after 5 minutes, where samples collected at 8 hours post dose removed 29-46%. As time of collection after dosing increased the percent dose removed from the skin decreased. Conversely, the lipophilic washing solutions, removed 68-95% of the dose for all study collection times [181]. The test compound used had an octanol-water partition coefficient value of 5.22 [182], which falls in the range of the 16 priority PAHs of 3.3 – 6.3.

The use of lipophilic substances to increase wipe collection efficiency has since been utilized by studies evaluating dermal exposure to PAHs and the practice has continued

[47, 48, 170, 171, 172, 174]. Väänänen and coworkers used seed oil as a wetting agent in wipe sampling for PAH collection in road pavers [171]. Boeniger and coworkers used corn oil as a wetting agent in tandem with wipe sampling for assessing dermal exposure to PAHs [170]. Multiple studies by Fent and coworkers applied corn oil to the skin prior to wipe sampling to assess firefighter's dermal exposure to PAHs during controlled training exercises [47, 48, 174].

Table 8: Decontamination of [14C]-MDI as Percent Dose Recovered [Mean (\pm SD)] in Skin Washes Following Topical Administration in Rhesus Monkeys [181]

Washing Methods	5 min	1 hour	4 hours	8 hours
Water	60 (11.1)	56.7 (10.1)	40.2 (8.9)	29.2 (9.7)
5% Soap	71.2 (5.2)	51.1 (14.1)	46.1 (8.2)	36.6 (12.8)
50% Soap	67.3 (9.6)	68.6 (16.0)	54.4 (5.2)	45.7 (6.6)
Polypropylene glycol	88.9 (13.5)	86 (14.1)	78.9 (16.4)	71.6 (19.7)
PG-C	85.3 (9.5)	67.7 (24.6)	73.7 (3.0)	77.9 (20.6)
Corn oil	95.1 (9.0)	77.2 (24.2)	73.2 (17.4)	86.2 (10.0)

Boeniger and coworkers have also investigated specific wipes for PAH exposure assessment using automotive repair technicians [170]. Of the two wipes used in the study, the Whatman filter paper media had a higher absolute PAH recovery from the hands than Alpha wipes, however, both wipes had incomplete recovery of PAHs. This finding was unexpected as the Alpha wipes sampling media possessed several physical attributes that suggested improved performance over the Whatman filter paper [170]. The unexpected outcome was hypothesized to be a result of the variability of the wiping method as samples were collected by individuals, changes in pressure, time and speed that could have affected the recovery. Reinforcing the importance of consistency during wipe sample collection.

Regarding the use of decontamination wipes for removing fireground contaminants there have only been two wipe manufacturers to publish some form of data. One of the earliest wipe manufacturers to publish data on their wipes, tested wipe effectiveness at removing [tris(2-chloroethyl)phosphate] (TCEP), benzo[a]pyrene, and lead [183, 184]. These studies all report high levels of contaminant recovery, with an average recovery greater than 85%, 79%, and 95%, respectively. The second decontamination wipe study assessed the ability of their wipe to remove dioxins and PAHs from different surfaces [185]. The test surfaces used included polycarbonate plastic, rubber, and skin, although the type of skin, whether animal or human, from where and how the skin was sourced was never mentioned. The average removal percentage was reported to be $\geq 90\%$ for all chemicals except 2,3,4,7,8 PeCDF – Pentachlorodibenzofuran. The researchers of this study concluded that De-Wipes can remove dioxins and PAHs from the skin.

However, there are significant problems with these two studies regarding their test procedures and relevancy to their end use. In one wipe manufacturer study used a “textured board” to simulate human skin, which grossly misrepresents the complexity, metabolic processes, and absorption mechanisms of human skin. Another wipe manufacturer study stated they used “skin,” but never stated how it was sourced, obtained, or maintained, making it a substantial source of potential error. Both studies used liquid chemicals in conjunction with non-porous surfaces. This combination results in the liquid chemical remaining on the surface making it easier to collect using a wipe, inflating a wipe’s ability to remove chemicals from a porous surface like skin. Furthermore, liquid chemicals are unrepresentative of the chemicals that fire service members are likely to encounter. The results from the Hero Wipes and De-Wipe studies can be misleading because fire service members are more likely to encounter soot and particulate matter, which have different rates of dermal absorption.

2.8.3. Substrate Contamination Methods

Wipe sampling methods often struggle finding realistic and reproducible methods to contaminate substrate surfaces. This difficulty is highlighted as the need for standardized procedures for contaminating and sampling trace explosive particles from substrates surfaces has been elusive [180, 186, 187]. Currently, there are three major methods used to contaminate a surface: solution deposition, dry transfer deposition, and ink jet printing.

2.8.3.1. Solution Deposition

The easiest method to apply a chemical contaminant to a substrate is by solution deposition, which applies a specific amount of analyte in a solvent and allows the solvent to evaporate. Solution deposition is also referred to as direct deposition in the literature but will be referred to as solution deposition in this review. There are several disadvantages of solution deposition. When applying particles to a substrate surface particle size and shape are difficult to recreate with solution deposition since substrate surfaces have unique wetting properties or solubility with respect to the solvent [180, 186]. Additionally, a porous or rough surface in combination with solution deposition may produce particle deposits in between fibers or openings by capillary action making them inaccessible to surface wiping, leading to lower collection efficiencies than if the particles were on the surface [180, 188]. Solution deposition is also well-known for leaving behind “coffee ring” traces where the analyte was applied to the substrate surface. These “coffee rings” are produced when the solvent evaporates leaving behind

a concentrated area of analyte which is generally undesirable [180]. Figure 28 illustrates the uneven distribution of particles when using solution deposition methods, thus resulting in the “coffee ring” phenomenon. Lastly, solution deposition on certain surfaces will not realistically mimic the deposition patterns of particulate matter potentially exaggerating the difficulty in sampling substrate surfaces [180]. In scenarios such as fire response, surface contaminants, like soot and particulates, settle from the environment or are physically transferred by means of contact to a substrate.

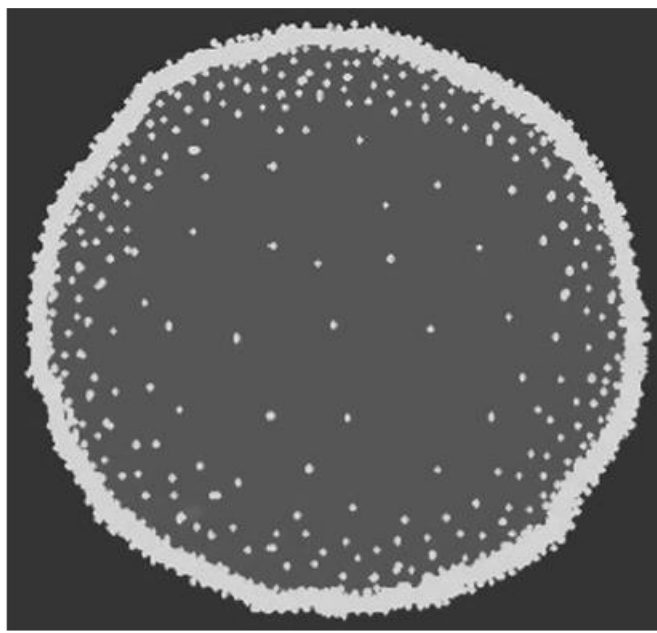


Figure 28: Illustration of solution deposition resulting in "coffee ring" phenomenon. The coffee ring phenomenon is characterized by a nonuniform distribution of particles with a higher concentration at the periphery of the droplet [189]

2.8.3.2. Dry Transfer Deposition

Alternatively, dry transfer deposition may serve as a better method to contaminate a surface. Dry transfer deposition is a rather simple method of applying a particulate analyte to a substrate surface by physical contact.

Dry transfer deposition has been used to transfer illicit drugs and trace explosives to substrate surfaces for testing collection methods. One method (US patent 6,470,730) has been developed by Transportation Security Labs to test for explosive particulate collection [186, 188]. Generally, the method is done by suspending an analyte of interest in water or volatile carrier

compatible with the analyte. The suspension liquid is deposited on a transfer surface and allowed to dry, where typical dry times last 24 hours [188]. After drying, the analyte of interest is in the form of a layer of normal size granules that can be transferred to the surface of the test substrate by rubbing, preventing the problem with liquid deposition where the analyte can settle in the openings of the substrate surface [188]. Even though dry transfer deposition method allows particles to be placed on the surface without wicking of the sample, there are drawbacks.

The time to dry the suspension can take up to twenty-four hours becoming quite tedious. When the suspension does dry fine particles may nucleate along the edge of the drying droplet, leaving behind remnants of fine particles distributed in the dry area of the droplet. When transferring these particles from the transfer material to the substrate of interest, the particles can be smeared and damaged if excessive force is used. Additionally, excessive pressure can push the particles into any available openings, making them unavailable for wipe sampling [186].

The two methods of substrate contamination, dry transfer deposition and solution deposition, were evaluated and compared to fingerprint contamination for trace explosive particles by Miller and Yoder [186]. They tested the transfer of royal demolition explosive (RDX), a popular explosive material used in laboratory studies, onto different substrates, shown in Figure 29. The study reinforced the difficulties of solution deposition. Reporting that droplets were found to spread to areas of roughness on the painted metal surface, difficulties in wipe sampling as the solvent wicked into the textile substrate surfaces, and the particles became embedded into rough areas on the surface. Conversely, the dry transfer technique was able to deposit particulates on the surface without wicking of the sample, however, the particles were smeared during transfer to the substrate. The smoother substrate surfaces like 50/50 cotton/polyester did not have as many crystals on the surface as the rougher substrates like leather. In conclusion, solution and dry transfer deposition contamination methods have limited control and lack a reproducible method of contaminant placement. The ideal contamination method would be able to place particulates in a precise and even manner across the surface of the substrate surface.

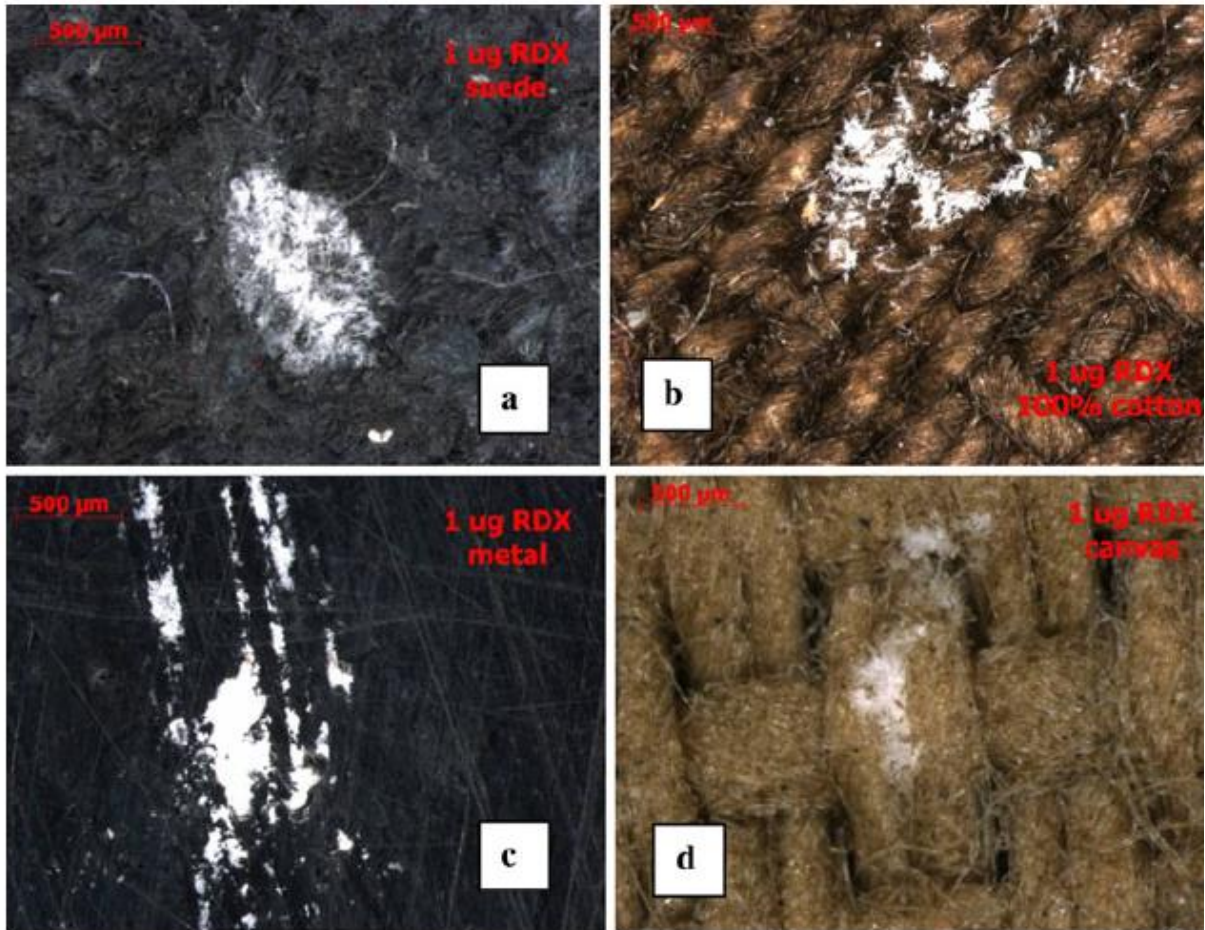


Figure 29: Microscopic photographs of RDX dry transfer onto (a) suede leather, (b) 100% cotton, (c) car hood, (d) 100% cotton canvas material [186]

2.8.3.3. Inkjet Printing

The struggle to apply particles on substrate surfaces in a controlled and measurable manner proves to be difficult by means of solution deposition or dry transfer deposition. One contamination method that may have the best attributes from both previous methods discussed would be drop-on-demand inkjet printing, with the added benefit of extreme precision and accuracy.

Inkjet printing systems can be broken down to a combination of three fundamental components: the solution being printed, the print engine or printhead, and the substrate being printed on [190]. The printhead is operated by a computer and can deposit droplets 1 – 100 µm in diameter depending on the system [180, 190]. In drop-on-demand (DOD) inkjet systems, droplets are created by applying a pressure pulse within an ejection chamber that feeds a nozzle,

shown in Figure 30, and are ejected when needed. Drop-on-demand inkjet printing provides precise control over the amount of analyte applied to a surface, accurate at picoliter volumes [180]. For example, it can accurately deposit a specific number of droplets while controlling the array of where droplets are added [191]. Furthermore, it can control deposit size and shape to some extent and is compatible with a variety of substrates [180, 191]. Several types of particles have been produced by DOD inkjet printing systems, including pure particles of cyclotrimethylenetrinitramine 10-30 μm in diameter, and ammonium nitrate particles of 40 μm in diameter [191].

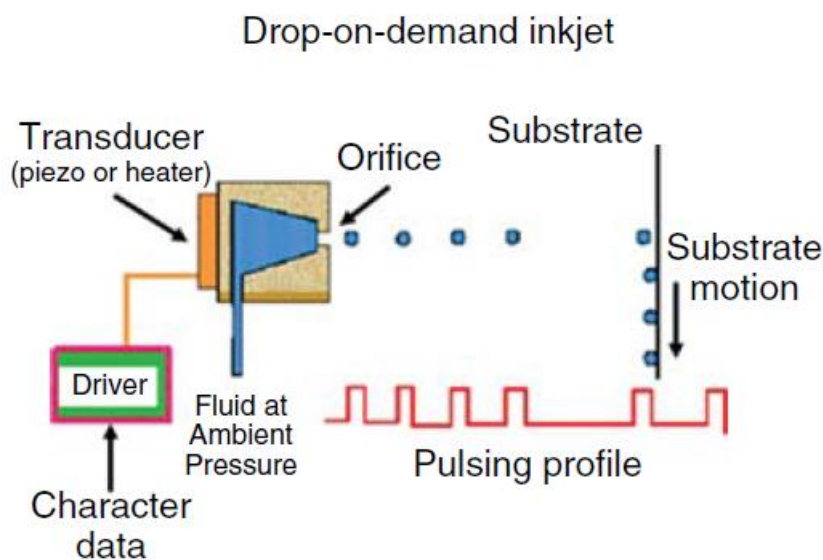


Figure 30: Illustration of the components in a Drop-on-Demand Inkjet Printing system [190]

Many variables can impact the drop; therefore, optimized parameters are needed to achieve the best drop at a sufficient velocity. Controlling the physical properties (size/volume) of the dispensed micro-drops and the ability to do so is particularly important, as these parameters will ultimately affect droplet variation and reproducibility. Verkouteren and coworkers (2017) used DOD inkjet printing to print RDX particles (1 – 40 μm) arrays onto polytetrafluoroethylene substrates, then transferred by rubbing onto target surfaces [180]. Holthoff and coworkers (2012) demonstrated control, sample uniformity, and reproducibility using inkjet printing obtaining a

calibration curve with an R^2 value of 0.991 and RSD value of less than 5%. Thus, demonstrating a precision and control offered by DOD inkjet printing sample preparation [187].

Albeit inkjet printing can produce extremely detailed arrays. There are some difficulties that can arise when using an inkjet printing system. The solvent used in the system must be compatible with the printer and primarily the viscosity and vapor pressure of the solvent must fall within a narrow window of compatibility [191]. Low viscosities can lead to satellite formation and residual pressure wave interaction between droplets. Conversely, high viscosities cause energy dissipation and hinder the formation of droplets. Furthermore, the evaporation rate of the solvent is quite sensitive. If evaporation occurs too quickly, the analyte may crystallize within the inkjet nozzle, ultimately growing into a blockage. If evaporation occurs too slowly, droplet formation becomes unstable. The issues and difficulties of using an inkjet printing system are not dissimilar to solution or dry transfer deposition. Thus, having precise control and precision of applying particulate contaminants to a substrate surface inkjet printing has a significant advantage over solution and dry transfer contamination methods.

Chapter 3: Percutaneous Absorption of Naphthalene, Phenanthrene, Benzo[a]pyrene, and Orthophenylphenol in the Porcine Skin Model

Abstract

Occupational exposures from firefighting have been determined to be a known carcinogen by the International Agency for Research on Cancer. Numerous studies have documented firefighters' exposures to carcinogens including polycyclic aromatic hydrocarbons (PAHs), volatile organic compounds, phthalates, flame retardants, and several more chemicals. This study was aimed at understanding firefighters' potential dermal absorption of fireground contaminants.

Three PAH compounds (naphthalene, phenanthrene, benzo[a]pyrene) and one known skin penetrating compound (orthophenylphenol) were tested *in vitro* to investigate their absorption into porcine skin in an artificial sweat dosing vehicle. Multiple absorption characteristics were calculated including cumulative absorption, percent dose absorbed, diffusivity, flux, lag time, and permeability. These absorption characteristics gave insight into the absorption behavior of fireground chemicals that firefighters would typically be exposed to. The absorption of the PAHs tested was influenced by their molecular weight. Naphthalene had the greatest dose absorption efficiency (35.0 ± 4.6 % dose), followed by the three-member ring phenanthrene ($6.8 \pm 3.2\%$ dose), and lastly the five-member ring benzo[a]pyrene had the lowest absorption ($0.03 \pm 0.04\%$ dose). Similarly, the lag time was influenced by the size of the penetrating chemical.

Naphthalene had the shortest lag time (52 ± 8 minutes), followed by phenanthrene (183 ± 21 minutes), and benzo[a]pyrene appeared to never reach steady state, so lag time was not determined. The absorption of orthophenylphenol ranked in between naphthalene and phenanthrene ($30.1 \pm 9.5\%$ dose absorbed, 103 ± 18 minutes lag time). Lipophilic chemicals like benzo[a]pyrene are less likely to penetrate the skin when an aqueous dose vehicle is used. Lastly all chemicals had a lag time of approximately 60 minutes or longer, meaning that if firefighters can clean their skin immediately after fire extinguishing activities, they may be able to remove fireground contaminants from the skin thus reducing their chemical exposures.

Keywords: Dermal Absorption, Polycyclic Aromatic Hydrocarbon, Porcine Skin, Synthetic Skin Membrane

Highlights

- Molecular weight appears to be a primary factor in the role of dermal absorption.
- It may be possible to remove polycyclic aromatic hydrocarbons from the skin after fire response, indicated by their long lag times.
- Sweat may reduce the absorption of lipophilic chemicals through the skin during fire response

3.1. Introduction and Background

On the fireground, there are numerous types of chemical hazards to which firefighters may be exposed to during fire response. Toxic fireground chemicals range from gaseous carbon monoxide and hydrogen cyanide, to the particulate matter found in the soot and smoke, to polycyclic aromatic hydrocarbons (PAHs), and several others not mentioned [47, 50, 173, 192]. Multiple studies have associated multiple types of cancers such as, but not limited to, multiple myeloma, non-Hodgkin lymphoma, prostate cancer, kidney cancer, and lung cancer to firefighting [61, 64, 65, 110]. In 2022, the International Agency for Research on Cancer (IARC) determined that the occupational exposure of firefighting is a Group 1 threat, meaning it is a known human carcinogen, based on “sufficient” evidence for mesothelioma and bladder cancer and “limited” evidence for colon cancer, prostate cancer, testicular cancer, melanoma of the skin, and non-Hodgkin lymphoma in humans [62]. In an effort to reduce cancer rates, the fire service industry is calling for research to increase understanding around firefighter exposures during fire suppression activities, post fire activities, and while living in the fire station.

There are three main routes of exposure in which firefighters can be exposed to toxic fireground contaminants. These routes include inhalation, dermal absorption, and ingestion. Inhalation is the most prioritized exposure pathway to protect against because of the lungs’ sensitivity and several fireground contaminants directly cause adverse respiratory effects. However, when a self-contained breathing apparatus (SCBA) is worn properly respiratory chemical exposures can be significantly reduced [193]. The second route of exposure of primary concern is dermal absorption. This is the most difficult exposure pathway to assess because of the variability in exposure between individuals and the difficulties in sampling contaminants from the skin [47, 192]. Due to these difficulties the dermal absorption pathway is not well understood. Ingestion is the final route of exposure, although it is often considered as the pathway that contributes the least to firefighter chemical exposures. However, improper cleaning practices and handling of gear can lead to cross contamination, potentially resulting in increased chemical exposures via the ingestion pathway [50].

Polycyclic aromatic hydrocarbons are a common fireground and environmental contaminant [24, 50, 53, 173]. Out of the hundreds of unique PAH compounds, sixteen have been deemed as priority chemicals by the Environmental Protection Agency (EPA) based on their abundance, toxicity, and potential for exposure [94]. These are frequently generated as

complex mixtures via the incomplete combustion of materials including crude oil, motor fuel, wood, and manufacturing processes such as the distillation process of coal into coke or coal tar and crude oil maturation [85, 194]. Exposure to PAHs has been associated with reproductive, developmental, and hemato-, cardio-, neuro-, and immunotoxicity effects [194]. Laboratory-based animal studies (pig, guinea pig, rat, and monkey) demonstrate that PAHs can penetrate the skin and be absorbed into the body. A common trend across several studies is the absorption of lower molecular weight PAHs (2-3 rings) is generally greater than higher molecular weight PAHs (4+ rings) [195, 196, 197].

During fire response it is extremely difficult to entirely avoid exposures to PAHs. These compounds have been found on the outside/inside of firefighter turnout gear, in air samples, on the skin of firefighters, and in biological samples taken from firefighters after fire response activities [47, 52, 173, 174, 198]. During training scenarios PAH concentrations have been observed as high as 2700 $\mu\text{g}/\text{m}^3$ in air samples and up to 355 $\mu\text{g}/\text{m}^3$ inside the turnout ensemble [52]. PAH concentrations on the skin have been found to be as low as $<4.5 \text{ ng}/\text{cm}^2$ and as high as 1200 ng/cm^2 [47, 199, 200]. Areas at the greatest risk for chemical deposition are areas of the body correlated with the interface areas of the turnout (i.e., neck, wrist, and forehead). Overall, studies have shown that the level of exposure for individuals is dependent on several factors such as fuel source, fire dynamics, and fire response tactics. However, job duty (i.e., inside search vs outside command) appears to play a significant role in the average level of chemical exposure [47, 201].

This study aims to understand the percutaneous absorption of PAHs in human skin during fire response. Three different PAHs, naphthalene, phenanthrene, and benzo[a]pyrene were exposed to porcine skin in an artificial sweat dosing vehicle in a flow through diffusion cell system. Porcine skin was used instead of human skin because it is easily obtainable and has been shown to perform similar to human skin in absorption studies [202, 203, 204]. The three PAHs selected include a 2-ring, 3-ring, and a 5-ring compound and span the range of size and properties of the EPA's 16 priority PAHs. The dosing vehicle in dermal absorption studies is typically an organic solvent or a solvent that allows for the test compound to dissolve. However, an artificial sweat dosing vehicle was selected to better mimic the sweat that would be on the skin of firefighters during fire response. The goal of this study is to generate data to better understand the absorption of PAHs in human skin under fire response conditions so that the fire

service industry can identify more effective protocols to reduce, mitigate, or eliminate firefighter exposures.

3.2. Methodology and Materials

3.2.1. Chemicals

Test chemicals ^{14}C -naphthalene (specific activity = 57 mCi/mmoL), ^{14}C -phenanthrene (specific activity = 55 mCi/mmoL), ^{14}C -benzo[a]pyrene (specific activity = 26.6 mCi/mmoL), and ^{14}C -orthophenylphenol (specific activity = 150 mCi/mmoL) were obtained from American Radiolabeled Chemicals (Saint Louis, MO, USA). Chemical properties of the radiolabeled chemicals can be seen in Table 9. Artificial eccrine perspiration (pH=4.5 stabilized with bactericide and fungicide), an artificial sweat, was used as the dosing vehicle and obtained from Pickering Laboratories (USA). The cells used for the flow through experiment were 9mm (0.64 cm²) in-line diffusion cells obtained from PermeGear (USA). The collection media was made up the day before the experiment and frozen overnight. Ingredients for the collection media included: bovine serum albumin fraction V (2.25% w/v), sodium chloride (0.3% w/v), potassium chloride (0.018% w/v), calcium chloride (0.014% w/v), potassium phosphate monobasic (0.008% w/v), magnesium sulfate (0.015% w/v), sodium bicarbonate (0.14% w/v), dextrose (0.06% w/v), distilled water (96.94% v/v), sodium heparin (0.25% v/v), amikacin (0.0063% v/v), and penicillin G sodium (0.0025% v/v) (Millipore Sigma, USA).

Table 9: Chemical properties of radiolabeled compounds used in flow through experiments

Compound	Naphthalene	Phenanthrene	Benzo[a]pyrene	Orthophenylphenol
Formula	C ₁₀ H ₈	C ₁₄ H ₁₀	C ₂₀ H ₁₂	C ₁₂ H ₁₀ O
CAS Number	91-20-3	85-01-8	50-32-8	90-43-7
Molecular Weight	128.2	178.2	252.3	170.21
Number of Aromatic Rings	3	4	5	2
Specific Activity (mCi/mmol)	57	55	27	150
Concentration (mCi/mL)	0.1	0.1	0.1	0.1
Solvent	Ethanol	Ethanol	Toluene	Ethanol
Log K _{ow}	3.30 ^a	4.46 ^a	6.13 ^a	3.09 ^a
Vapor Pressure (mmHg at 25°C)	8.5 x 10 ⁻²	1.2 x 10 ⁻⁴	5.5 x 10 ⁻⁹	2.0 x 10 ⁻³
Solubility in Water at 25°C (mg/L)	31 ^a	1.10 ^a	1.62 x 10 ^{-3 a}	0.7 ^a
Radioactivity	1 - ¹⁴ C	9 - ¹⁴ C	7 - ¹⁴ C	Ring - ¹⁴ C
^a Values obtained from Hazardous Substances Data Bank				

3.2.2. Flow Through Diffusion Cell Set Up

The flow through diffusion cell system, described by Bronaugh and Stewart [205], was used to perfuse porcine skin membranes. Fresh porcine skin was obtained from Yorkshire/Landrace pigs (20 – 60 kg). The pigs were shaved and dermatomed to a thickness of 200-300 µm with an electric dermatome (Padgett Instruments, Kansas City, MO, USA). Afterwards, each piece of skin was cut into a circular disk, placed into the diffusion cell, and secured in place, providing a dosing surface area of 0.64 cm². The porcine skin membranes were dosed within 30 minutes of death of the porcine skin donor, so skin integrity testing was not necessary [206].

The underside of the skin disks was perfused with a bovine serum albumin collection media and maintained at a pH between 7.3 and 7.6. The temperature of the perfusate and diffusion cells were maintained at 37°C ± 1°C using a heating block. The flow rate was maintained at 4 mL h⁻¹ using a peristaltic pump. The room temperature and relative humidity

were recorded throughout the experiment for record keeping. Perfusate samples were collected in glass scintillation vials at times: 0, 15, 30, 45, 60, 75, 90, 120, 180, 240, 360, and 480 minutes. After the flow-through diffusion cell systems were set up the chemical doses were added to each cell. The time for the experiment and sample collection started immediately after the last cell was dosed.

3.2.3. Dosing Procedure

Test chemicals ^{14}C -naphthalene, ^{14}C -phenanthrene, ^{14}C -benzo[a]pyrene, and ^{14}C -orthophenylphenol were made into separate dose mixtures. Each dosing solution was prepared by adding the test chemical to the artificial sweat and then adding acetone (1% of total volume). Each dosing solution was vortexed to ensure the test compound was thoroughly mixed. Skin disks were dosed with 100 μL of the respective dosing solution administered through a delivery channel to the top of the cell. Applying either 1.6 $\mu\text{g}/\text{cm}^2$ (0.5 μCi) of NAP (n=4), 7.8 $\mu\text{g}/\text{cm}^2$ (1.5 μCi) of PHEN (n=5), 36.0 $\mu\text{g}/\text{cm}^2$ (2.5 μCi) of BAP (n=5), and 2.0 $\mu\text{g}/\text{cm}^2$ (1.1 μCi) of OPP (n=5). After dosing, diffusion cells were covered with Parafilm® pieces (Pechiney Plastic Packaging, IL, USA) to minimize the loss of semi-volatile compounds.

3.2.4. Sample Analysis

Perfusate samples were taken at time points: 0, 15, 30, 45, 60, 75, 90, 120, 180, 240, 360, and 480 minutes after dosing. After the experiment, aliquots of the perfusate were transferred to new scintillation vials along with 15 mL of BioScint (National Diagnostics, GA, USA) and analyzed using a liquid scintillation counter for ^{14}C determination. At the end of the experiment the remaining dose was removed from the surface of the skin membrane with a cotton swab. The skin membranes were transferred to wax paper, where the surface of each skin disk was then tape-stripped (Scotch Tape; 3M, St. Paul, MN, USA) six times, placing three strips into a single scintillation vial, and adding 10 mL of ethyl acetate. After tape-stripping the center of the skin disks were punched with an 8mm biopsy tool, the center and peripheral skin were separated and placed into individual scintillation vials along with 2 mL of BioSol. The skin samples were incubated at 50°C for 8 – 12 hours and analyzed using a liquid scintillation counter for ^{14}C determination. The fingertips of the gloves used during swabbing and tape stripping were extracted with ethanol.

3.2.5. Absorption Calculations

Absorption was defined as the total percentage of dose detected in the perfusate. Cumulative absorption ($\mu\text{g cm}^{-2}$) was calculated by summing the total dose that was detected in the perfusate at each sampling time. Flux ($\mu\text{g cm}^{-2} \text{hr}^{-1}$) was obtained from the steady-state slope of the cumulative absorption versus time curves, example provided in Figure 31. The permeability coefficient (K_p) (cm hr^{-1}) was calculated from the ratio of the flux ($\mu\text{g cm}^{-2} \text{hr}^{-1}$) to the concentration (C_s) ($\mu\text{g cm}^{-3}$) of the dose. The dose concentration was obtained from 10- μL pre- and post-dose checks. The lag time (τ) was obtained by extrapolated the steady-state portion of the curve back to the time- or x-axis. This lag time was related back to diffusivity (D) and membrane thickness (L) by the following equation: $D=L^2/6(\tau)$. Student's t-tests were performed to determine significant differences at $P < 0.05$. Statistical tests were performed for several absorption characteristics on two compounds at a time as each compound had unique chemical properties. Statistical tests with results are listed in Table 10.

Table 10: Test for statistical differences using student-t tests ($p < 0.05$) for absorption characteristics of PAH compounds and OPP in porcine skin using an artificial sweat dosing vehicle

Comparison	Flux (% Dose/hr)	Flux ($\mu\text{g}/\text{cm}^2/\text{hr}$)	Cumulative Absorption ($\mu\text{g}/\text{cm}^2$)	Absorption Efficiency (% Dose)	Diffusivity (cm^2/hr)	Permeability (cm/hr)	Lag Time (minutes)
NAP vs PHEN	YES	NO	NO	YES	YES	YES	YES
NAP vs BAP	YES	N/A	YES	YES	N/A	N/A	N/A
NAP vs OPP	YES	YES	NO	NO	YES	YES	YES
PHEN vs BAP	YES	N/A	YES	YES	N/A	N/A	N/A
PHEN vs OPP	YES	NO	NO	YES	YES	YES	YES
BAP vs OPP	YES	N/A	YES	YES	N/A	N/A	N/A

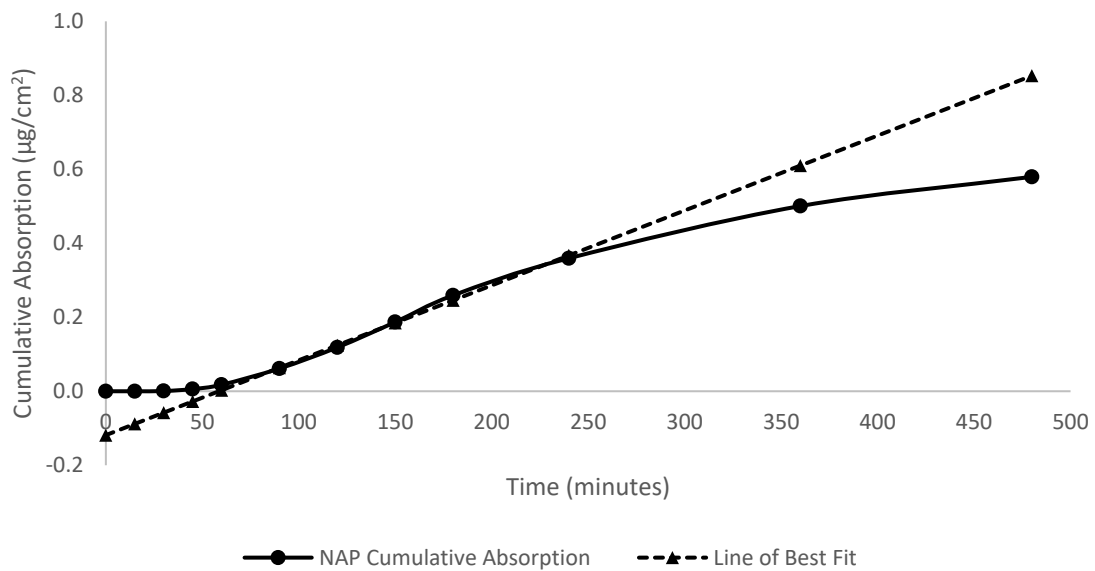


Figure 31: Cumulative absorption ($\mu\text{g cm}^{-2}$) versus time (hr) plot for naphthalene in artificial sweat following topical application to porcine skin *in vitro* flow through diffusion cells. The best-fit line was used to calculate the flux for the test compounds.

3.3. Absorption Results

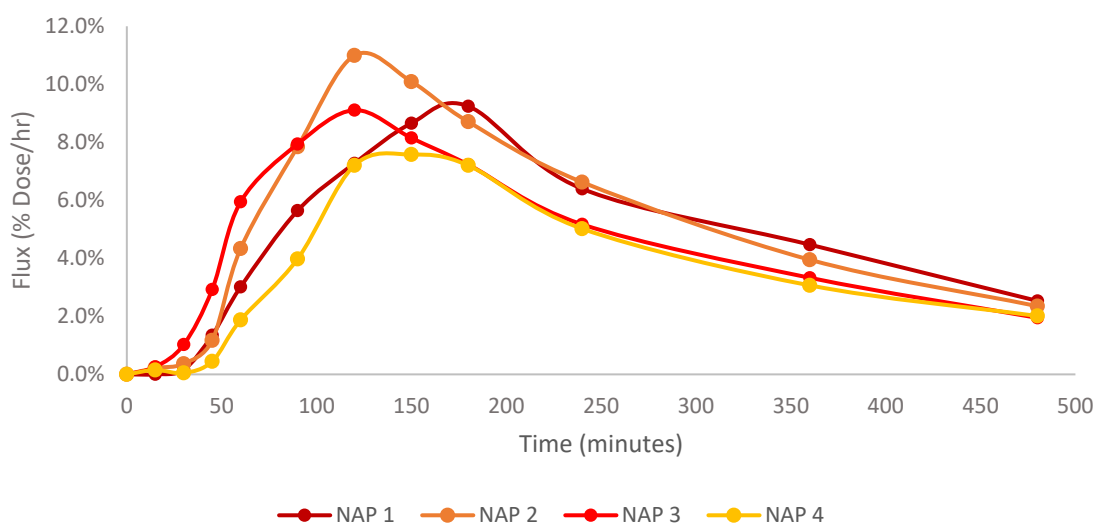
3.3.1. Dermal Absorption, Flux, Diffusivity, and Permeability

Upon initial inspection of the dermal absorption data of NAP, PHEN, and BAP there was a potential outlier in the data, cell BAP 2. The Grubbs' test was used to determine if the seemingly atypical value was indeed an outlier. After testing the Grubbs' test showed that the cell was indeed an outlier for flux ($p < 0.01$), cumulative absorption ($p < 0.01$), and permeability ($p < 0.01$). As a result, the outlier was excluded from all calculations. The unusual BAP value may have been due to damage to the skin caused during skin collection, through handling when setting up the experiment, or misalignment in the diffusion cell creating an opening that was not observed. Damage to the skin would reduce the barrier properties and result in increased absorption.

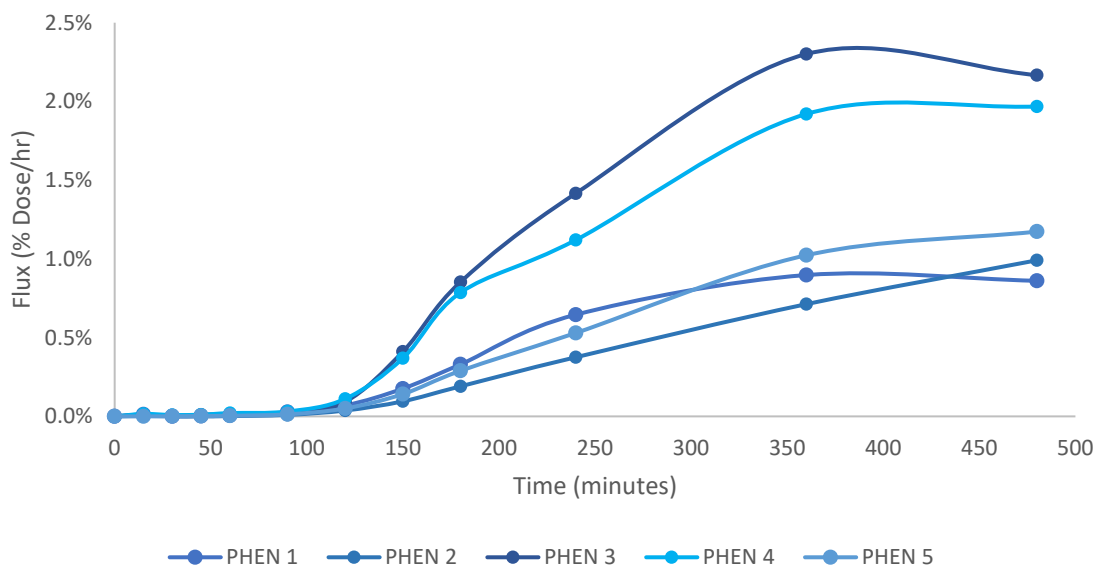
The flux of each PAH compound was unique, shown in **Error! Reference source not found.**, and is representative of the different properties unique to each of them. Naphthalene had the greatest peak flux ranging from 7.6 – 11.0% dose/hr, phenanthrene had a peak flux ranging from 0.9 – 2.3% dose/hr, benzo[a]pyrene had a peak flux ranging from 0.002 – 0.02% dose/hr. The flux of orthophenylphenol was similar to phenanthrene and had a peak flux ranging from 3.9 – 6.9% dose/hr. Naphthalene reached steady state within 52 ± 8 min, phenanthrene reached steady state within 183 ± 21 min, and orthophenylphenol reached steady state within 103 ± 18 min. Due to the low absorption of benzo[a]pyrene it was determined that the lag time of benzo[a]pyrene could not be calculated accurately and therefore was not included.

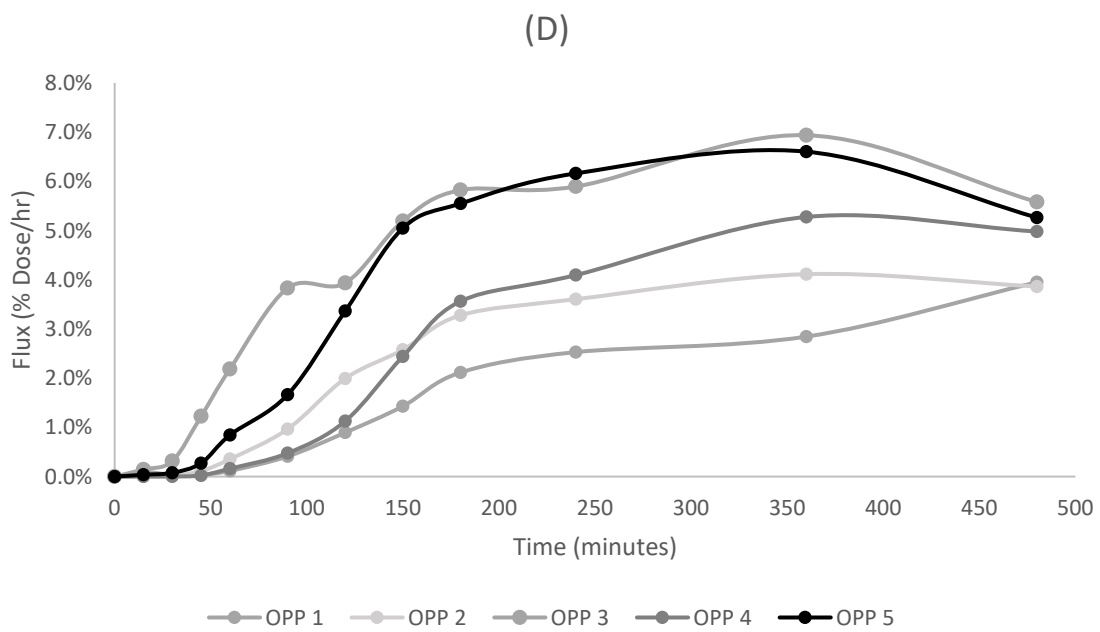
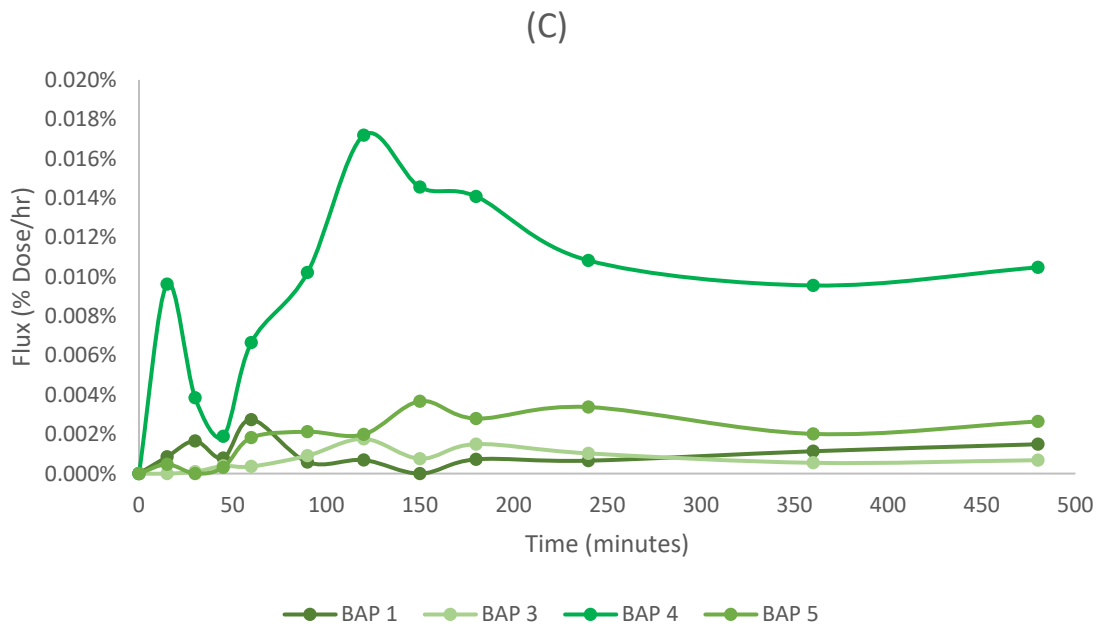
Figure 33: Flux (% Dose/hr) versus time (hr) plot for (A) naphthalene, (B) phenanthrene, (C) benzo[a]pyrene, and (D) orthophenylphenol in artificial sweat following topical application to porcine skin in vitro flow through diffusion cell.

(A)



(B)

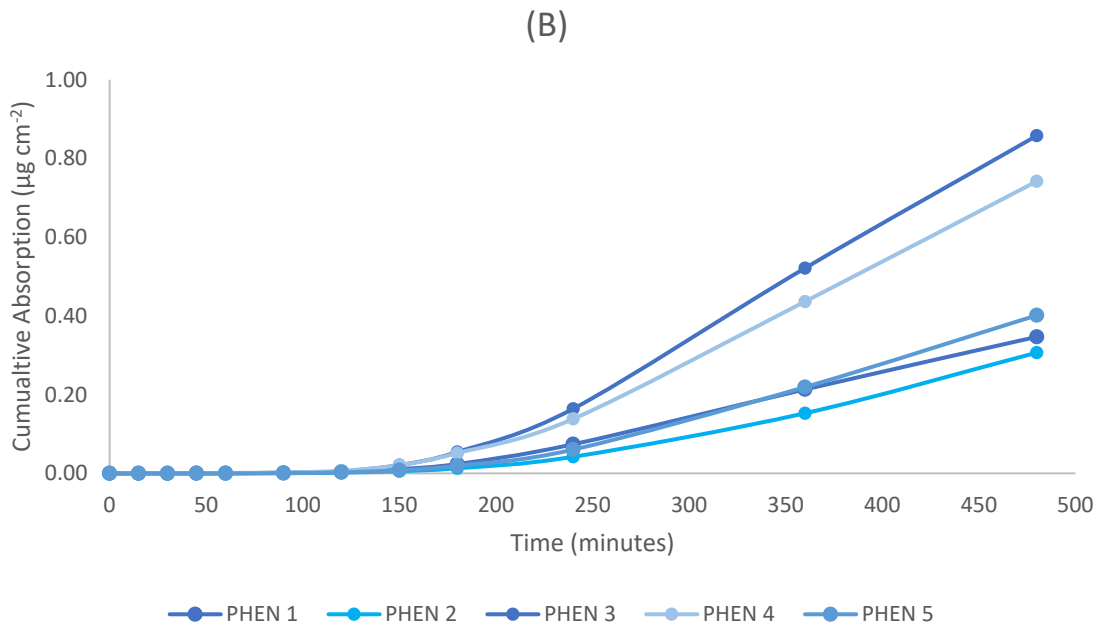
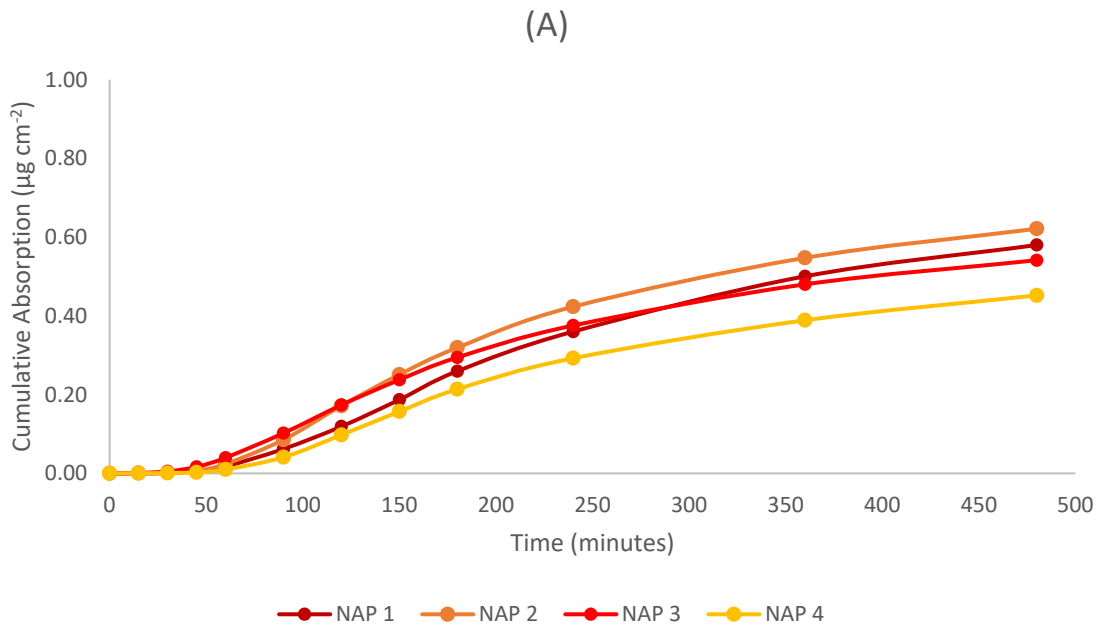


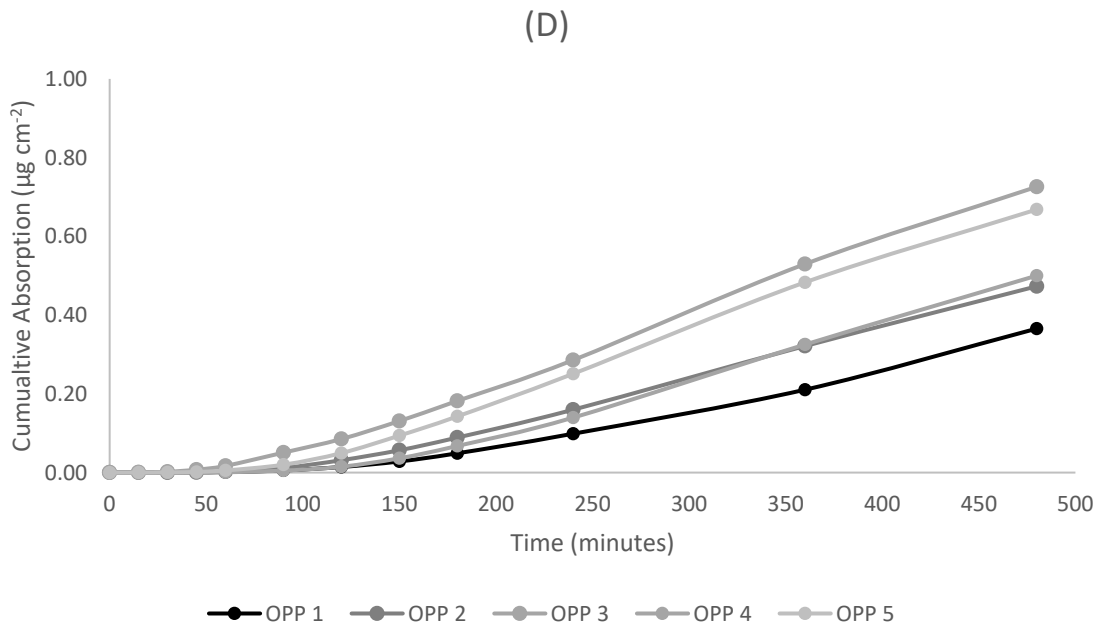
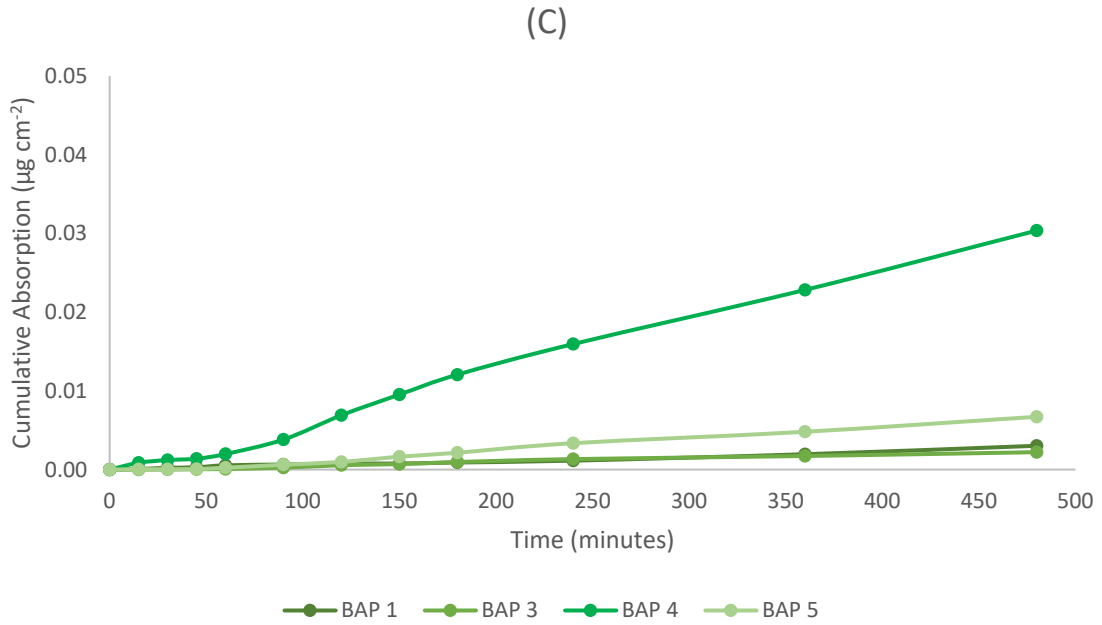


The cumulative absorption ($\mu\text{g cm}^{-2}$) of the PAH compounds were 0.55 ± 0.07 , 0.53 ± 0.25 , and 0.011 ± 0.013 for naphthalene, phenanthrene, and benzo[a]pyrene, respectively. The cumulative absorption of orthophenylphenol was 0.55 ± 0.15 , which was similar to the absorption of naphthalene and phenanthrene. As seen in Figure 32 the absorption of benzo[a]pyrene was significantly lower than phenanthrene and naphthalene. However, the low absorption of may be explained by the insolubility of benzo[a]pyrene in the artificial sweat vehicle. To further investigate the effect of the artificial sweat dosing vehicle the experiment should be repeated with other vehicles, for example neat, ethanol, or acetone.

There was no significant difference ($p < 0.05$) in cumulative absorption ($\mu\text{g cm}^{-2}$) between naphthalene, phenanthrene, and orthophenylphenol. However significant differences were observed when comparing the dose absorption efficiency (% dose absorbed). The cumulative percent dose absorbed for naphthalene, phenanthrene, benzo[a]pyrene, and orthophenylphenol was $35.0 \pm 4.6\%$, $6.8 \pm 3.2\%$, $0.03 \pm 0.4\%$, and $30.1 \pm 9.5\%$ dose respectively, illustrated in Figure 33. When looking at absorption in this context there are significant differences between all three PAH compounds and between orthophenylphenol and phenanthrene ($p < 0.05$). As listed in Table 11: Summary of the Absorption Parameters (Mean \pm Standard Deviation), Lag Time (minutes), Flux ($\mu\text{g cm}^{-2} \text{ hr}^{-1}$), Diffusivity ($\text{cm}^2 \text{ hr}^{-1}$), and Permeability (cm hr^{-1}) Table 11, significant differences ($p < 0.05$) were observed for lag time, flux, and permeability across NAP, PHEN, and OPP.

Figure 32: Cumulative Absorption ($\mu\text{g cm}^{-2}$) versus time (minutes) for (A) naphthalene, (B) phenanthrene, (C) benzo[a]pyrene, and (D) orthophenylphenol in artificial sweat following topical application to porcine skin in vitro flow through diffusion cell.





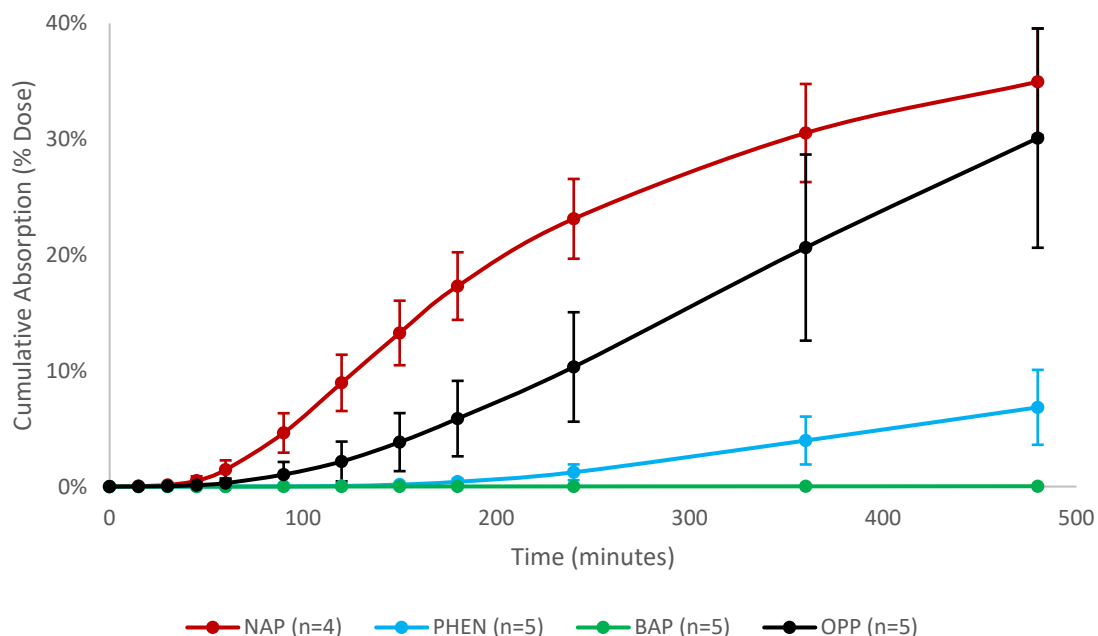


Figure 33: Average cumulative absorption (% dose) versus time (hr) plot for naphthalene, phenanthrene, benzo[a]pyrene, and orthophenylphenol in artificial sweat following topical application to porcine skin in vitro flow through diffusion cell (error bars are standard deviation).

Table 11: Summary of the Absorption Parameters (Mean \pm Standard Deviation), Lag Time (minutes), Flux ($\mu\text{g cm}^{-2} \text{hr}^{-1}$), Diffusivity ($\text{cm}^2 \text{hr}^{-1}$), and Permeability (cm hr^{-1}) of PAHs in porcine skin

	Naphthalene	Phenanthrene	Benzo[a]pyrene	Orthophenylphenol
Lag Time (minutes)	52 \pm 8	183 \pm 21	*N/A	103 \pm 18
Flux x 10⁻² ($\mu\text{g cm}^{-2} \text{hr}^{-1}$)	12.4 \pm 2.2	10.4 \pm 4.5	*N/A	8.5 \pm 2.4
Diffusivity x 10⁻² ($\text{cm}^2 \text{hr}^{-1}$)	79.3 \pm 2.8	19.9 \pm 2.2	*N/A	42.2 \pm 8.5
Permeability (cm hr^{-1})	0.012 \pm 0.002	0.002 \pm 0.001	*N/A	0.007 \pm 0.002
Permeability x 10⁻³ (cm hr^{-1})	12.4 \pm 2.2	2.0 \pm 1.0	*N/A	7.3 \pm 2.4

*N/A: The absorption parameters for benzo[a]pyrene were not included due to the low amount of absorption and no clear steady state being reached. Therefore, it was deemed that if the absorption parameters were calculated they would be inaccurate.

3.3.2. Skin Penetration and Mass Balance

Overall, the total recovery for all compounds ranged from 94 – 102 % dose. Recovery exceeded 100% because calculations were based on dose values, which may include human error, compound evaporating, and error within the analytical instrument. While the majority of the dose was accounted for in either the absorption or swab samples there was some dose found in the tape strips and in the skin itself. Phenanthrene had the greatest amount of dose recovered in the skin ($32.4 \pm 5.2\%$ dose), followed by orthophenylphenol ($10.6 \pm 3.3\%$ dose), then benzo[a]pyrene ($1.8 \pm 1.8\%$ dose), and lastly naphthalene ($0.7 \pm 0.2\%$ dose). The lowest amounts of each compound were found in the stratum corneum. Phenanthrene had the greatest amount of dose recovered in the stratum corneum ($2.3 \pm 0.6\%$ dose), followed by orthophenylphenol ($0.3 \pm 0.3\%$ dose), then naphthalene ($0.1 \pm 0.1\%$ dose) and benzo[a]pyrene ($0.1 \pm 0.2\%$ dose).

Table 12: Mass Balance Summary of ^{14}C -Naphthalene, ^{14}C -Phenanthrene, ^{14}C -Benzo[a]pyrene, and ^{14}C -Orthophenylphenol in porcine skin

	Naphthalene	Phenanthrene	Benzo[a]pyrene	Orthophenylphenol
Dose ($\mu\text{g}/\text{cm}^2$)	1.6	7.8	36.0	2.0
Swab (% Dose)	60.3 ± 4.5	56.6 ± 3.5	98.0 ± 2.1	56.4 ± 11.7
Stratum Corneum (% Dose)	0.1 ± 0.1	2.3 ± 0.6	0.1 ± 0.2	0.3 ± 0.3
Skin (% Dose)	0.7 ± 0.2	32.4 ± 5.2	1.8 ± 1.8	10.6 ± 3.3
Absorption (% Dose)	35.0 ± 4.6	6.8 ± 3.2	0.03 ± 0.04	30.1 ± 9.5
Total Recovery (% Dose)	96.1 ± 1.2	98.1 ± 3.3	100.0 ± 2.2	97.4 ± 3.0

3.4. Discussion

Dermal absorption is a complex concept to predict due to the numerous biological factors of the skin, physicochemical properties of the penetrating chemical, interactions between the penetrating chemical and dosing vehicle, and the environment factors that influence both the skin and the penetrating chemical. Researched factors that have been shown to influence percutaneous penetration include the molecular weight of the penetrating chemical, the partition coefficient ($\log K_{ow}$) value, and the dosing vehicle [137, 207].

The Dalton 500 rule is a general predictor of a chemicals' ability to penetrate the skin. It states that chemicals with a molecular weight less than 500 Dalton can easily pass through the stratum corneum, but as the molecular weight of a chemical increased their absorption rapidly declines [137]. All PAH compounds that were tested were below the 500 Dalton threshold and were expected to penetrate the skin. Each PAH was observed to penetrate the skin and as the size of the compound increased absorption decreased. Naphthalene had the greatest percent dose absorbed, followed by the middle-sized PAH phenanthrene, and the largest PAH benzo[a]pyrene had the lowest. The decrease in absorption as molecular weight increased followed the trend of the 500 Dalton rule.

In addition to molecular weight, the octanol-water partition coefficient is a prevalent indicator of a chemical's ability to penetrate the stratum corneum [207]. The octanol-water partition coefficient is the ratio that represents the equilibrium distribution of a chemical between an organic solvent and water. For a chemical to penetrate the skin it may navigate the lipophilic (lipid bilayers, sebaceous glands, cell membranes, etc.) or hydrophilic (amino acids, blood capillaries, aquaporins, etc.) parts to penetrate through the skin and the octanol-water partition coefficient has been used to predict a chemical's behavior. Generally, substances with higher log K_{ow} values are more lipophilic and have an increased ability to penetrate the skin's lipid layers, leading to higher absorption. Conversely, substances with lower K_{ow} values are more hydrophilic and may have a more challenging time crossing the skin barrier. Chemicals with a log K_{ow} greater than -1 and less than 4 are expected to have high rates of absorption and chemicals outside the previously mentioned range are expected to have approximately 10% absorption [208]. Surprisingly, As the log K_{ow} of the chemicals used in this experiment increased, the percent dose absorbed decreased. Naphthalene and orthophenylphenol have log K_{ow} values of 3.30 and 3.09, respectively, and had the highest percent dose absorbed. Phenanthrene has a log K_{ow} value of 4.46 and had significantly lower percent dose absorbed compared to the chemicals with lower log K_{ow} values. The decrease in percent-dose absorbed was even greater for benzo[a]pyrene which has a log K_{ow} value of 6.13. If absorption were predicted strictly using the log K_{ow} values it would be expected for benzo[a]pyrene to have the greatest absorption, followed by phenanthrene, and then naphthalene. However, other characteristics and interactions can greatly influence the percutaneous absorption of a substance.

The dose vehicle refers to the carrier or medium used to administer a chemical or test substance to an experimental subject, such as an animal, membrane, or cell culture. The choice of dose vehicle is vital because it can significantly influence the behavior, solubility, and bioavailability of the test substance. The primary goal of selecting an appropriate dose vehicle is to ensure accurate and consistent dosing of the test substance while minimizing any potential interference with the biological effects being studied. The artificial sweat dosing vehicle is unlike traditional organic solvent dosing vehicles more commonly used in *in vitro* chemical absorption studies. Organic solvent dosing vehicles are typically the solvent of choice for dermal absorption studies for two reasons; first they enhance the solubility of wide range of substances, and second they evaporate quickly from the surface of the skin, helping to maintain a constant concentration of the penetrating chemical on the surface of the skin and reducing any dose vehicle – chemical interactions [208]. It is important to emphasize that the selection of the artificial sweat dosing vehicle used in this study was selected to mimic the sweat on the skin that would be present on the skin of firefighters during fire response. This study was intended to understand the dermal absorption during a worst-case scenario of a fireground contaminant contacting a firefighter's skin.

The percutaneous absorption of the three PAHs tested in this study have been studied with naphthalene being the most studied, followed by benzo[a]pyrene, while there are fewer studies on the phenanthrene. The majority of studies on the dermal absorption of naphthalene have looked at the absorption through jet fuel mixtures.

The data generated from this study aligns with previous percutaneous absorption studies for naphthalene and phenanthrene. Several studies have tested the percutaneous absorption of naphthalene from jet fuel mixtures where flux ($\mu\text{g cm}^{-2} \text{hr}^{-1}$) values have ranged from 0.156 – 0.376 in porcine skin and 0.45 in human skin [209, 210]. Permeability values generated from studies that used jet fuel mixtures to dose naphthalene ranged from $1.14 - 1.81 \times 10^{-4}$ in porcine skin, $5.12 \pm 2.88 \times 10^{-3}$ in monkey skin, and 2.17×10^{-4} in human skin [209, 210, 211]. Frasch et al. (2007) exposed NAP to hairless guinea pig skin and reported flux values of 30.39 ± 2.03 and 7.52 ± 4.68 when using a powder and 13.61 ± 4.54 when using an aqueous vehicle [212]. Permeability values were not determined for the powder exposures due to complications when using a particulate vehicle. However, the permeability value for the aqueous vehicle was reported to be $0.478 \pm 0.149 \text{ cm hr}^{-1}$, which is multiple orders of magnitude higher than the

permeability values reported in jet fuel studies. The flux and permeability values for naphthalene generated in this study, 0.129 ± 0.021 and 0.031 ± 0.005 , fall in between the values reported by previous studies.

The percutaneous absorption of phenanthrene was investigated by Sartorelli et al. (1998) in vitro using monkey skin and an acetone dosing vehicle. The permeability value (cm/hr) was reported to be $0.00196 \pm 0.00114 \times 10^{-3}$, comparable to the value reported in this study 0.00219 ± 0.001 [211].

The absorption of benzo[a]pyrene in this study was generally minimal, less than 1% of the dose absorbed. This is lower than values reported in previous absorption studies of BAP. Moody et al. (1995) examined the absorption of BAP in multiple animal species and in human skin. They reported absorption values of 51.1 ± 0.9 % dose in rat, 27.5 ± 1.3 % dose in guinea pig, 3.3 ± 0.7 % dose in human skin 32-year-old, and 1.5 ± 0.6 % dose in human skin 50-year-old [197]. Ng et al., (1992) reported similar BAP absorption values in guinea pig, 6% dose at 6 hours and 37% dose at 24 hours (dose 8.1 ug , 32.1 nmol/cm^2) [105]. However, the importance of the dosing vehicle for BAP was highlighted by Wester et al., (1990), when using soil and acetone vehicle, the absorption of BAP dropped from 23.7 ± 9.7 % dose when an acetone vehicle was used to 1.4 ± 0.9 % dose when a soil vehicle was used. This was then repeated in a monkey skin model where absorption from an acetone vehicle was significantly higher than from a soil vehicle, 51.0 ± 13.2 % dose and 13.2 ± 3.4 % dose, respectively [103]. Peckham et al., (2017) conducted a similar study exposing BAP with various soils and acetone. This study also found that BAP absorption when using a soil vehicle (weathered or unweathered) was less than when an acetone vehicle was used [102]. In addition to the role of the dose vehicle the receptor solution was shown to greatly increase BAP absorption by Yang et al., (1986) where they reported absorption values of 0.14 ± 0.04 % dose absorbed in rat skin 350 μm thick when using a saline receptor solution and were able to increase absorption when changing the combination between skin thickness and receptor solution, obtaining increased absorption values of 1.6 ± 0.8 % and 17.2 ± 2.0 % dose absorbed in 24 hours, with full thickness and nonionic surfactant receptor solution and 350 μm thick skin and nonionic surfactant receptor solution, respectively [104].

Again, the absorption of BAP in this study was lower than in previous studies. In all previous studies an acetone dosing vehicle was used, whereas in this study an artificial sweat

vehicle was used. The artificial sweat dosing vehicle is unlike the traditional organic solvent dosing vehicles more commonly used in chemical absorption studies. Organic solvent dosing vehicles are typically the solvent of choice for dermal absorption studies because they increase penetration by evaporating from the surface of the skin and leave the penetrating chemical on the surface, thus eliminating any dose vehicle–chemical interactions [208].

The data from these flow through experiments indicate that sweat may play a role in decreasing the absorption of more lipophilic contaminants. The high octanol-water partition coefficient value of benzo[a]pyrene (6.13) indicates it has a low affinity for aqueous environments, such as the artificial sweat, so it may be possible for benzo[a]pyrene to have fallen out of solution and dissociate to the surface of the sweat dose vehicle. Furthermore, artificial sweat is less volatile than acetone and would take significantly longer to evaporate and may not evaporate when the diffusion cell is occluded, like in this study. The lack of evaporation of the dose vehicle combined with the low solubility of BAP would suggest that there is minimal to no contact with the skin, thus reducing the degree of absorption that may occur. The low degree of absorption of benzo[a]pyrene indicates that sweat may play a role in decreasing the absorption of more lipophilic contaminants.

3.5. Conclusions

For firefighters and other first responders who work near fire scenes it is expected that exposure to fireground contaminants is imminent. Several studies have quantified PAH levels on personal protective equipment and clothing as well as skin. Absorption of low molecular weight PAH compounds is likely to occur if they encounter skin. Whereas the absorption of higher MW and lipophilic PAH compounds is less likely to penetrate the sweat and absorb into skin, making sweat an additional layer of protection against chemical absorption. Regardless, to minimize chemical exposures, firefighters should clean their skin as soon as possible in an attempt to remove any contaminants before they penetrate the skin.

It is well known that exposure to fireground contaminants is unavoidable for firefighters. Contaminants have been found on the clothing, equipment, and skin of firefighters and the risk of dermal absorption is high. This study indicates that PAH chemicals are capable of penetrating skin during fire response when the skin of firefighters is sweating. Lower molecular weight PAHs are more likely to penetrate the skin during fire response than higher molecular weight PAHs due to the aqueous properties of sweat and the low solubility of high molecular weight

PAHs in sweat. PAH exposure may be reduced if the chemical can be removed from the skin during the lag time of the chemical before it penetrates the skin. Therefore, it is recommended that firefighters clean their skin as soon as possible upon completing fire extinguishing activities and leaving the fire scene.

3.6. Acknowledgements

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Chapter 4: Impact of the Fireground Environment on the Percutaneous Absorption of Polycyclic Aromatic Hydrocarbons

Abstract

Firefighters often work in extreme environments that induce several physiological responses such as elevated body and skin temperature, sweating, and increased heart rate and respiration rate. Some of the physiological responses like increased heart rate, increased skin and core body temperature are believed to increase dermal absorption. These physiological responses are further exacerbated by the heavy equipment worn to protect against thermal hazards. Even after short bouts of fire response firefighters are often covered in sweat as the body attempts to cool itself. The role of sweat on dermal absorption has yet to be investigated. After post-fire suppression activities firefighters may clean their skin with a decontamination wipe. However, firefighters have expressed concern over the ingredients used in the decontamination wipes increasing dermal absorption. This study is aimed at understanding the effect of skin temperature and potential effects of decontamination wipes on the percutaneous absorption of a polycyclic aromatic hydrocarbon (phenanthrene) *in vitro*. The effect of skin temperature was tested at three different temperatures 32°C, 37°C, and 40°C. The effect of decontamination wipes was tested by extracting decontamination wipes and adding it to the skin after dosing. A 2.4-fold increase in flux (% dose/hr) was observed when the temperature was increased from 32°C to 37°C and a 1.6-fold increase from 37°C to 40°C. No significant change in the lag time going from 32°C to 37°C was observed, but there was an approximate 30-minute decrease in lag time going from 37°C to 40°C. No penetration enhancement effects were observed in any of the wipes tested, rather cumulative absorption decreased with the addition of wipe solution. Slight differences in cumulative absorption among two pairings of wipes, wipes 1 and 3 vs wipes 2 and 4, were observed. Firefighters should monitor their exposure to extreme temperatures to minimize the increase in body and skin temperature. Decontamination wipes are unlikely to increase dermal absorption and should be used upon exiting the fire scene to remove any chemicals remaining on the skin before they can be absorbed.

Keywords: *Dermal Absorption, Polycyclic Aromatic Hydrocarbon, Porcine Skin, Fireground, Decontamination Wipe*

Highlights:

- Dermal absorption increased when skin temperature is increased
- Decontamination wipes appear to have no enhancement effect on the absorption of phenanthrene
- There were no significant differences between decontamination wipes on dermal absorption

4.1. Introduction and Background

Firefighters are almost guaranteed to be exposed to fireground contaminants during firefighting activities. Studies have characterized firefighter exposures to polycyclic aromatic hydrocarbons (PAHs) during training exercises, fire response, overhaul, and automobile fires [53, 174, 213, 214]. PAH concentrations in air samples have been found to exceed either published ceiling values, short term exposure limits, or NIOSH recommended exposure limits [24]. Furthermore, PAHs have been found on the gear and skin of firefighters after fire response as high as 600 $\mu\text{g}/\text{cm}^2$ and 313 $\mu\text{g}/\text{m}^2$ respectively [47]. Occupational exposures to PAHs are correlated with increased incidence of lung, skin, and bladder cancers [215]. Animal studies have shown that PAH exposure can also interfere with the hematopoietic, immune system causing reproductive, neurologic, and developmental effects [215].

When a chemical comes into contact with skin it may penetrate the stratum corneum (the protective barrier of the skin) and be absorbed into the body. It is well known that PAHs can penetrate the skin, but firefighters' dermal exposures are still not well understood. Exposure can occur through several routes such as vapors and gases, direct deposition of particulate matter onto the skin after exposure to smoke, walking through soot, and cross contamination through handling contaminated gear. Furthermore, the act of firefighting is often done under extreme temperatures causing physiological responses that may change the barrier properties of skin, thus making it difficult to predict an individual's chemical exposure. Firefighter heart rates can increase to 67 – 83% of their max heart rate by wearing their entire protective ensemble, which is exacerbated during fire response and exposure to extreme temperatures [34, 35, 36]. Increased heart rate will result in increased blood flow and uptake rate of drugs and/or chemicals, meaning a greater amount of PAHs can be absorbed into the blood and distributed throughout the body. Under the physical burden of the turnout gear and extreme temperatures of fire response it is estimated that firefighters may sweat as much as 50 – 70 oz in 30 – 45 minutes of fireground. However, the evaporative cooling experience through sweating is drastically reduced during fire response resulting in elevated skin and core body temperature, which have been recorded as high as 35 – 40+°C [34, 35, 36, 37, 38, 39, 40, 41]. Additionally, sweat may impact the dermal absorption of fireground contaminants potentially serving as an additional barrier that chemicals need to navigate before encountering skin. However, the increased temperature of the skin and body may increase absorption, which is explained by several theories, such as an increase in the

fluidity of the stratum corneum lipids leading to increase in intercellular space or by changes in the lipid viscosity causing a state transition in the lipids in the SC reported in both *in vivo* and *in vitro* chemical absorption studies [216, 217].

Although it is difficult to characterize dermal exposures there are several reasons why researchers believe it is a major exposure pathway for firefighters [218]. The first reason is that PAHs have been found on the gear and skin of firefighters [47, 53]. The second reason is the risk of cross-contamination. Firefighters may not clean or wash their gear while at the fire scene prior to returning to the station. When the contaminated gear is then stored and transported cross contamination secondary exposure is likely to occur [70]. The third reason is the condition the body is in during firefighting activities. Physiological responses such as sweating, increased heart rate, increased core and skin temperature are well documented when firefighters wear their turnout gear which are then exacerbated under fire response scenarios. The physiological responses that firefighters routinely experience have been studied for their effects on dermal absorption and suggest they likely increase chemical absorption [35, 37, 39, 41, 42, 43].

To mitigate chemical exposures firefighters are implementing on-scene decontamination strategies, such as wiping the skin with decontamination wipes after fire suppression activities. The goal of on-scene decontamination is to remove any contaminants that may be on the surface of the gear or skin of firefighters after fire scene exposure, thus reducing their chemical exposures. However, there is limited data on the effectiveness of decontamination wipe products on removing contaminants from the skin. Additionally, some firefighters have expressed concerns over some ingredients in the decontamination wipes that may potentially increase dermal absorption. These concerns are valid, for example, glycerin has been shown to be a penetration enhancer, furthermore, plant extracts, polysorbate 20, and citric acid may have the potential to serve as a penetration enhancer as well [219, 220, 221, 222]. However, the concentration of these ingredients in the decontamination wipe solutions may not illicit an effect. Therefore, investigation into the effect of decontamination wipes on dermal absorption is needed.

This study was designed to investigate the effects of temperature and whether the additive solution used in the decontamination wipes increase the dermal absorption of fireground contaminants. From the previous chapter, three different PAHs were tested, however due to issues with volatilization and minimal skin penetration of naphthalene and benzo[a]pyrene they were not used in these experiments, making phenanthrene as the benchmark compound for PAH

absorption. To investigate the effects that temperature had on dermal absorption phenanthrene was tested at three different temperatures 32°C, 37°C, and 40°C. To investigate the effects of using a decontamination wipe four different decontamination wipe products were extracted and their solutions were added to the diffusion cell to determine if there was an increase in the absorption of phenanthrene. The overall goal of this study is to improve the understanding of firefighter chemical exposures through dermal absorption to establish better firefighting and decontamination practices.

4.2. Methodology and Materials

4.2.1. Wipe Materials

Four different decontamination wipe products were selected to test the effects of the decontamination wipe solution on dermal absorption. Each wipe product was secured through their commercial vendors. Wipe solution was collected from each wipe by wringing it out by hand. The solution was then later administered to the diffusion cells. Multiple ingredients were found in several decontamination wipe products which included water, glycerol, plant extracts, caprylyl, tea tree oil, polysorbate 20, phenoxyethanol, sodium benzoate, citric acid, and several more. The ingredient lists of the wipes tested in this study can be found in Table 13.

4.2.2. Chemicals

Test chemical ^{14}C -phenanthrene (specific activity = 55 mCi/mmoL) was obtained from American Radiolabeled Chemicals (Saint Louis, MO, USA). Artificial eccrine perspiration (pH=4.5 stabilized with bactericide and fungicide), an artificial sweat, was used as the dosing vehicle and obtained from Pickering Laboratories (USA). The cells used for the flow through experiment were 9mm (0.64 cm²) in-line diffusion cells obtained from PermeGear (USA). The collection media was made up the day before the experiment and frozen overnight. Ingredients for the collection media included: bovine serum albumin fraction V (2.25% w/v), sodium chloride (0.3% w/v), potassium chloride (0.018% w/v), calcium chloride (0.014% w/v), potassium phosphate monobasic (0.008% w/v), magnesium sulfate (0.015% w/v), sodium bicarbonate (0.14% w/v), dextrose (0.06% w/v), distilled water (96.94% v/v), sodium heparin (0.25% v/v), amikacin (0.0063% v/v), and penicillin G sodium (0.0025% v/v) (Millipore Sigma, USA).

Table 13: Ingredient list of different decontamination wipe products

Wipe 1	Wipe 2	Wipe 3	Wipe 4
Water (Aqua)	Water	Deionized Water (Aqua)	Water
Hexylene Glycol	Propanediol	Gluconolactone	Phenoxyethanol
Glycerin	Aloe Barbadensis Leaf Extract	Decyl Glucoside	Decyl glucoside
Sodium Hydroxymethylglycinate	Chamomila Recutia (Matricaria) Flower Extract	Sodium Benzoate	Tetrasodium Glutamate Diacetate
Citric Acid	Cucumis Sativis (Cucumber) Fruit Extract	Dehydroacetic Acid	Sodium Benzoate
Disodium Cocoamphodiacetate	Althaea Officinalis Root Extract	Calcium Gluconate	Sodium Citrate
Fragrance	Avena Sativa (Oat) Kernel Extract	Caprylic/Capric Triglyceride	Citric Acid
Sodium Benzoate	Decyl Glucoside	Chamomilla Recrutia Extract	Sodium Bicarbonate
Potassium Sorbate	Polyglyceryl-10 Caprylate/Caprates	Aloe Barbadensis Extract,	Glycerin
Disodium Cocoyl Glutamate	Coco Glucoside	Tocopheryl Acetate (Vitamin E)	Tocopheryl Acetate (Vitamin E)
Sodium Cocoyl Glutamate	Glyceryl Oleate		Cucumis Sativus (cucumber) Fruit Extract
	Polysorbate 20		
	Tetrasodium Glutamate Diacetate		
	Trisodium Phosphate		
	Citric Acid		
	Caprylyl glycol		
	Benzalkonium Chloride		
	Sodium Benzoate		
	Potassium Sorbate		
	Phenoxyethanol		

4.2.3. Flow Through Diffusion Cell Set Up

The flow through diffusion cell system, described by Bronaugh and Stewart [205], was used to perfuse porcine skin membranes. Fresh porcine skin was obtained from Yorkshire/Landrace pigs (20 – 60 kg). The pigs were shaved and dermatomed to a thickness of 200-300 μm with an electric dermatome (Padgett Instruments, Kansas City, MO, USA). Afterwards, each piece of skin was cut into a circular disk, placed into the diffusion cell, and secured in place, providing a dosing surface area of 0.64 cm^2 . The porcine skin membranes were dosed within 30 minutes of death of the porcine skin donor, so skin integrity testing was not necessary [206].

The underside of the skin disks was perfused with a BSA collection media and maintained at a pH between 7.3 and 7.6. The temperature of the perfusate and diffusion cells were maintained at either $32^\circ\text{C} \pm 1^\circ\text{C}$, $37^\circ\text{C} \pm 1^\circ\text{C}$, or $40^\circ\text{C} \pm 1^\circ\text{C}$ using a heating block. The lower temperature was chosen because previous dermal absorption studies have used 32°C and the higher temperature was based on evidence of firefighter skin temperatures have been recorded as high as 40°C [40, 36, 35, 223, 38, 37, 39, 41]. The flow rate was maintained at 4 mL h^{-1} using a peristaltic pump. The room temperature and relative humidity were recorded throughout the experiment for record keeping. Perfusate samples were collected in glass scintillation vials at times: 0, 15, 30, 45, 60, 75, 90, 120, 180, 240, 360, and 480 minutes. After the flow-through diffusion cell systems were set up the chemical doses were added to each cell and occluded. The time for the experiment and sample collection started immediately after the last cell was dosed.

4.2.4. Dosing Procedure

^{14}C -phenanthrene was taken from the stock solution and made into a dose mixture (acetone 1% v/v), phenanthrene (15% v/v), and artificial sweat (84% v/v). The dosing solution was prepared by adding the test compound to the artificial sweat and then adding acetone (1% of total volume). The dose mixture was vortexed to ensure the test compound was thoroughly mixed. Skin disks were dosed with 100 μL to the top of the skin membrane, administering $4.6\text{ }\mu\text{g}/\text{cm}^2$ ($\sim 1.0\text{ }\mu\text{Ci}$) of phenanthrene in the temperature experiments and $9.0\text{ }\mu\text{g}/\text{cm}^2$ ($\sim 1.8\text{ }\mu\text{Ci}$) in the wipe solution experiments. Dose was determined by taking the average of 3 pre- and post-dose aliquots of 10 μL from the dosing solution. After dosing, diffusion cells were covered with Parafilm® pieces (Pechiney Plastic Packaging, IL, USA) to minimize the loss of semi-volatile

compounds. After 30 minutes of beginning the experiment 100 μL of wipe solution was delivered to the top of the skin.

4.2.5. Sample Analysis

Perfusate samples were taken at time points: 0, 15, 30, 45, 60, 75, 90, 120, 180, 240, 360, and 480 minutes after dosing. After the experiment, aliquots of the perfusate were transferred to new scintillation vials along with 15 mL of BioScint (National Diagnostics, GA, USA) and analyzed using a liquid scintillation counter for ^{14}C determination. At the end of the experiment the remaining dose was removed from the surface of the skin membrane with a cotton swab. The skin membranes were transferred to wax paper, where the surface of each skin disk was then tape-stripped (Scotch Tape; 3M, St. Paul, MN, USA) six times, placing three strips into a single scintillation vial, and adding 10 mL of ethyl acetate. After tape-stripping the center of the skin disks were punched with an 8mm biopsy tool, the center and peripheral skin were separated and placed into individual scintillation vials along with 2 mL of BioSol. The skin samples were incubated at 50°C for 8 – 12 hours and analyzed using a liquid scintillation counter for ^{14}C determination. The fingertips of the gloves used during swabbing and tape stripping were extracted with ethanol.

4.2.6. Absorption Calculations

Absorption was defined as the total percentage of dose detected in the perfusate. Cumulative absorption ($\mu\text{g cm}^{-2}$) was calculated by summing the total dose that was detected in the perfusate at each sampling time. Flux ($\mu\text{g cm}^{-2} \text{hr}^{-1}$) was obtained from the steady-state slope of the cumulative absorption versus time curves, example provided in Figure 34. The permeability coefficient (K_p) (cm hr^{-1}) was calculated from the ratio of the flux ($\mu\text{g cm}^{-2} \text{hr}^{-1}$) to the concentration (C_s) ($\mu\text{g cm}^{-3}$) of the dose. The dose concentration was obtained from 10- μL pre- and post-dose checks. The lag time (τ) was obtained by extrapolated the steady-state portion of the curve back to the time- or x-axis. This lag time was related back to diffusivity (D) and membrane thickness (L) by the following equation: $D=L^2/6(\tau)$. Statistical tests were performed for several absorption characteristics between the temperature groups (32°C , 37°C , and 40°C) and different wipes (No Wipe, Wipe 1, Wipe 2, Wipe 3, and Wipe 4). Statistical tests with results are listed in Table 14.

Table 14: Test for statistical significant differences using Anova and student-t tests ($p < 0.05$) for absorption characteristics of PHEN at different temperatures and with different decontamination wipe ingredients in porcine skin using an artificial sweat dosing vehicle

Comparison	Statistical Test	Flux (% Dose/hr)	Flux ($\mu\text{g}/\text{cm}^2/\text{hr}$)	Cumulative Absorption ($\mu\text{g}/\text{cm}^2$)	Absorption Efficiency (% Dose)	Diffusivity (cm^2/hr)	Permeability (cm/hr)	Lag Time (minutes)
32°C vs 37°C vs 40°C	Anova	YES	YES	YES	YES	YES	YES	YES
32°C vs 37°C	Student-T Test	YES	YES	YES	YES	YES	YES	YES
32°C vs 40°C	Student-T Test	YES	YES	YES	YES	YES	YES	YES
37°C vs 40°C	Student-T Test	NO	NO	NO	NO	NO	NO	NO
No Wipe vs Wipe 1 vs Wipe 2 vs Wipe 3 vs Wipe 4	Anova	YES	YES	YES	YES	YES	YES	YES
Wipe 1 vs Wipe 2	Student-T Test	YES	YES	YES	YES	YES	YES	YES
Wipe 1 vs Wipe 3	Student-T Test	NO	NO	NO	NO	NO	NO	NO
Wipe 1 vs Wipe 4	Student-T Test	YES	NO	NO	NO	YES	NO	YES
Wipe 2 vs Wipe 3	Student-T Test	YES	NO	NO	NO	NO	NO	NO
Wipe 2 vs Wipe 4	Student-T Test	NO	NO	NO	NO	NO	NO	NO
Wipe 3 vs Wipe 4	Student-T Test	NO	NO	NO	NO	YES	NO	YES
No Wipe vs Wipe 1	Student-T Test	YES	YES	YES	YES	YES	YES	YES
No Wipe vs Wipe 2	Student-T Test	YES	YES	YES	YES	YES	YES	YES
No Wipe vs Wipe 3	Student-T Test	YES	YES	YES	YES	YES	YES	YES
No Wipe vs Wipe 4	Student-T Test	YES	YES	YES	YES	YES	YES	NO

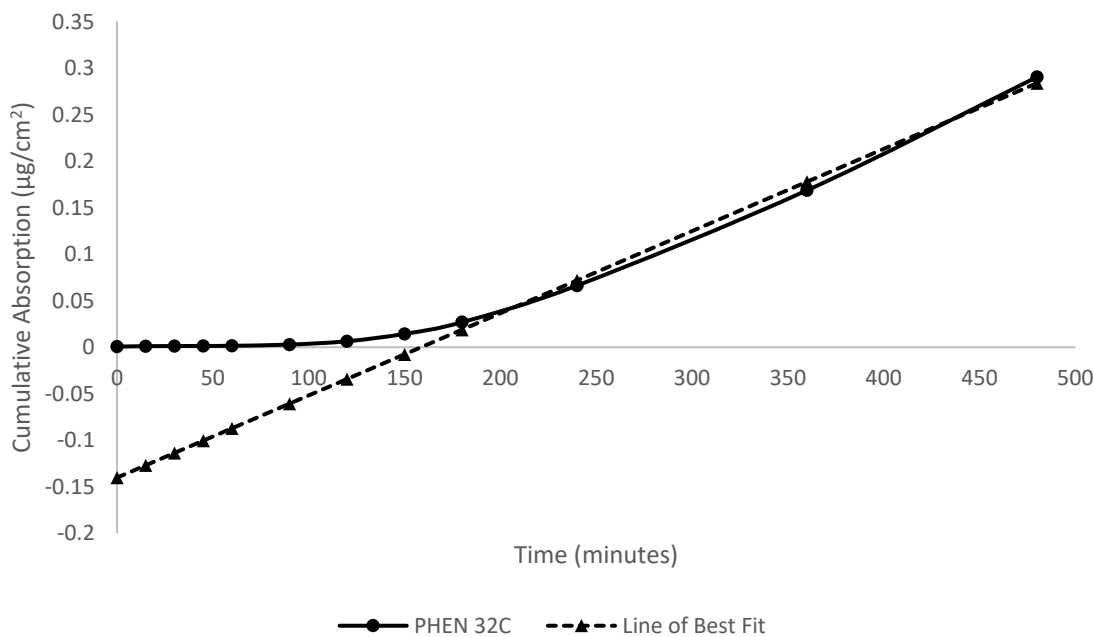


Figure 34: Cumulative absorption ($\mu\text{g cm}^{-2}$) versus time (hr) plot for phenanthrene at 32°C in artificial sweat following topical application to porcine skin *in vitro* flow through diffusion cells. The best-fit line was used to calculate the flux for the test compounds.

4.3. Results

4.3.1. Temperature Experiments

4.3.1.1. Dermal Absorption, Flux, Lag Time, Diffusivity, and Permeability

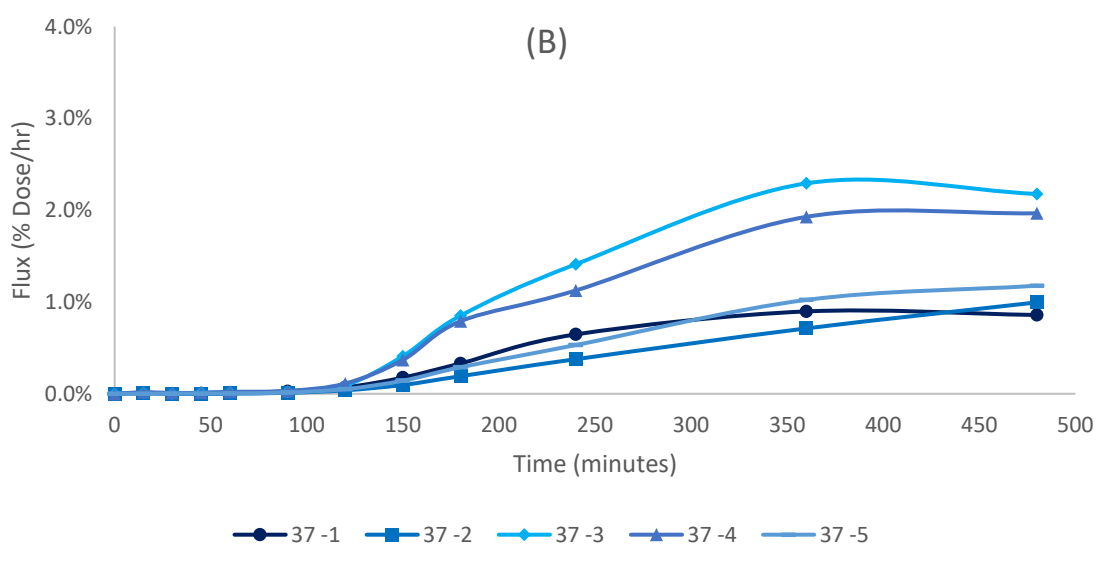
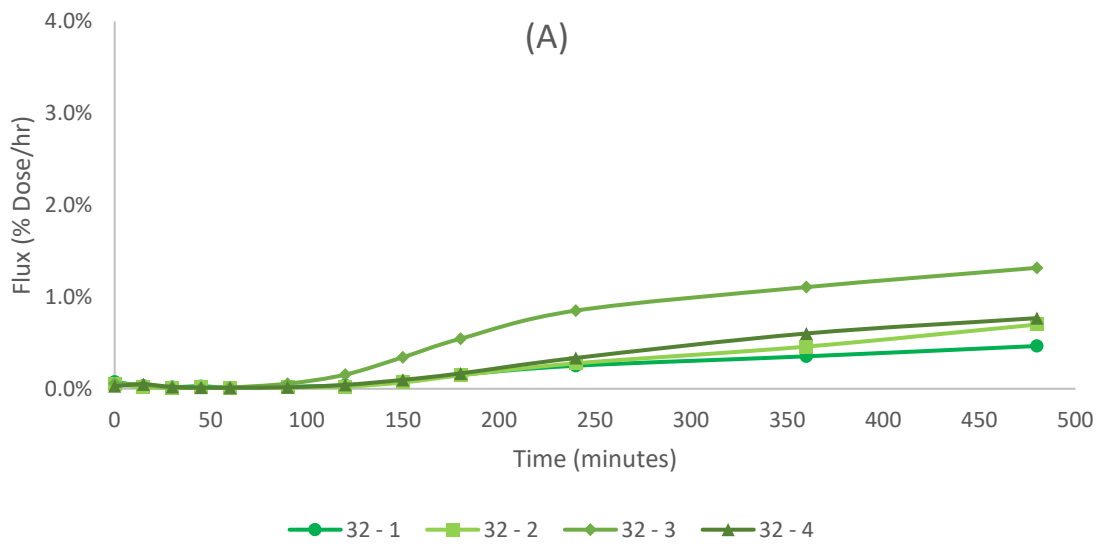
The flux (% dose/hr) of phenanthrene in porcine skin had significant differences at 32°C vs 37°C and 32°C vs 40°C , meanwhile 37°C vs 40°C had no significant differences ($p < 0.05$). This trend was also observed for cumulative absorption ($\mu\text{g cm}^{-2}$), absorption efficiency (% dose absorbed), flux ($\mu\text{g cm}^{-2} \text{ hr}^{-1}$), and permeability coefficient (cm hr^{-1}). A summary of these values can be found in Table 15. There were noticeable differences in peak absorption, 32°C (0.8% dose/hr), 37°C (2.3% dose/hr) and 40°C (3.7% dose/hr), increasing as temperature increased. Although there were no significant differences in absorption going from 37°C to 40°C , the absorption profiles in Figure 35 and Figure 36 illustrate that the average absorption increased as temperature increase. In general, the lag time decreased as temperature increased. Significant differences were observed between 37°C vs 32°C and 40°C , surprisingly no significant

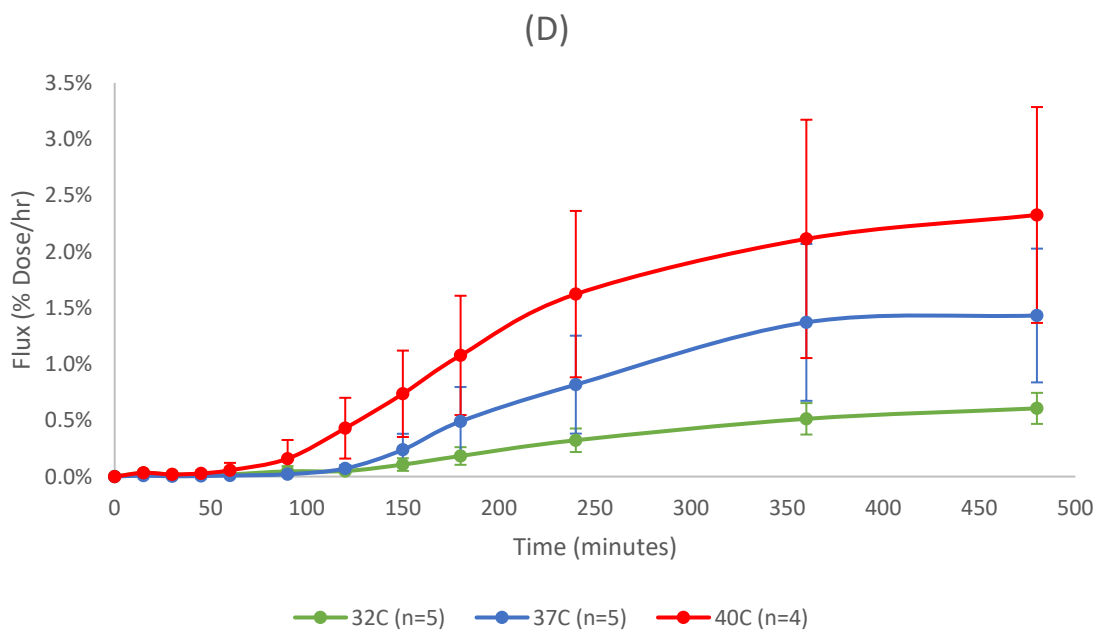
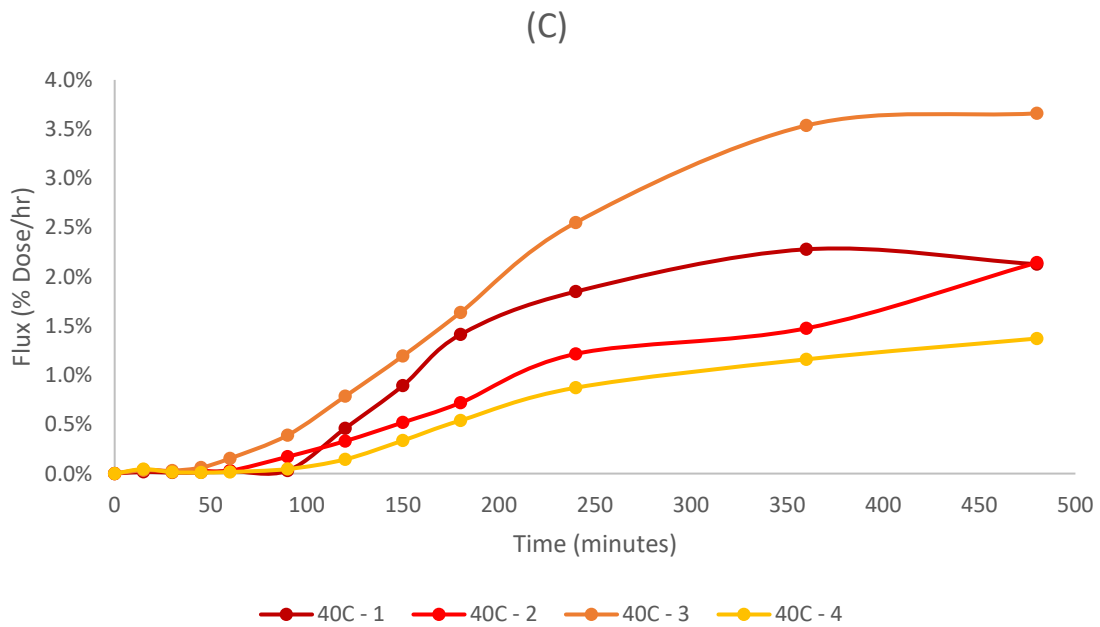
differences were observed between the lowest and highest temperatures. The same trend was observed for diffusivity. The significant differences for lag time and diffusivity may be explained by the differences in dose between 32°C and 40°C (4.6 $\mu\text{g}/\text{cm}^2$) vs 37C (7.8 $\mu\text{g}/\text{cm}^2$).

Table 15: Absorption characteristics of phenanthrene in porcine skin dosed at 32°C, 37°C, and 40°C applied in an artificial sweat dosing vehicle

Temperature	Cumulative Absorption ($\mu\text{g cm}^{-2}$)	Cumulative Absorption (% Dose)	Flux ($\times 10^{-2}$) ($\mu\text{g cm}^{-2}\text{hr}^{-1}$)	Lag Time (minutes)	Diffusivity ($\times 10^{-2}$) ($\text{cm}^2 \text{hr}^{-1}$)	Permeability ($\times 10^{-4}$) (cm hr^{-1})
32°C	0.13 \pm 0.03	2.8 \pm 0.7	2.6 \pm 0.6	186 \pm 12	32.9 \pm 1.9	8.8 \pm 2.0
37°C	0.53 \pm 0.25	6.8 \pm 3.2	10.4 \pm 4.5	183 \pm 21	19.9 \pm 2.2	21.0 \pm 9.1
40°C	0.54 \pm 0.25	11.7 \pm 5.4	9.9 \pm 4.4	155 \pm 9	39.3 \pm 0.8	33.6 \pm 14.7

Figure 35: Flux (% Dose/hr) profiles phenanthrene at different temperatures A) 32°C, B) 37°C, C) 40°C in an artificial sweat dosing vehicle in porcine skin *in vitro*. Graph D) compares the flux (% Dose/hr) of each temperature (error bars are standard deviation).





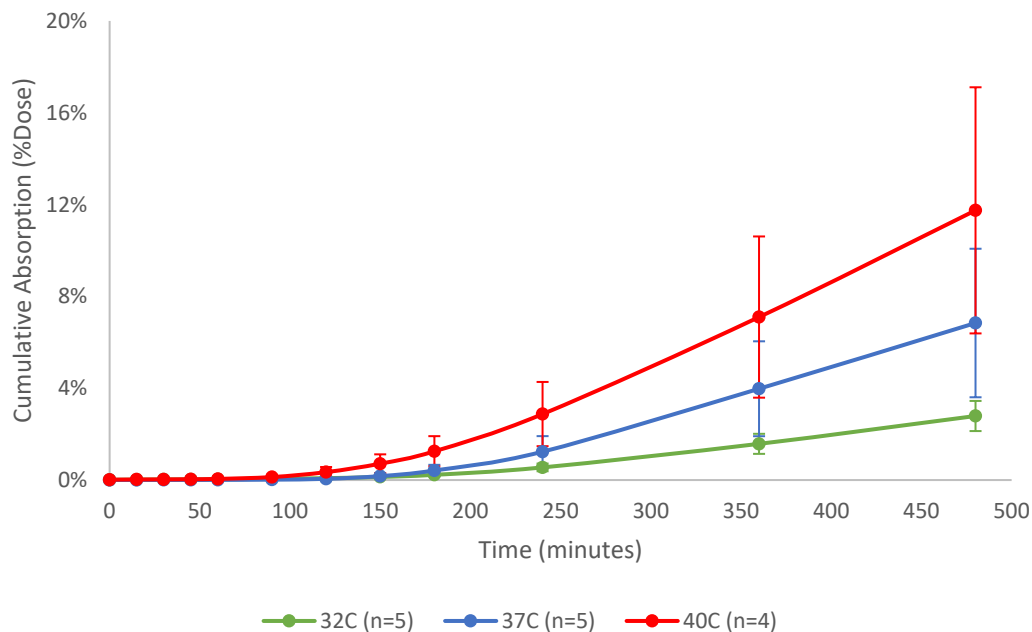


Figure 36: Cumulative Absorption (% Dose) profile of phenanthrene at 32°C, 37°C, and 40°C applied to the surface of porcine skin in an artificial sweat dosing vehicle (error bars are standard deviation).

Table 16: Phenanthrene recovered (average \pm standard deviation) from absorbed, skin, stratum corneum, and skin surface during temperature flow through experiments.

Temperature	Dose ($\mu\text{g cm}^{-2}$)	Absorption (% dose)	Skin (% dose)	Stratum Corneum (% dose)	Remaining Dose (% dose)	Total Recovery (% dose)
32°C	4.6	2.8 \pm 0.7	15.0 \pm 4.0	0.0 \pm 0.0	74.9 \pm 2.5	93.2 \pm 3.9
37°C	7.8	6.8 \pm 3.2	32.4 \pm 5.2	2.3 \pm 0.6	56.6 \pm 3.5	98.1 \pm 3.3
40°C	4.6	11.7 \pm 5.4	17.5 \pm 2.5	0.1 \pm 0.0	71.5 \pm 7.5	100.8 \pm 1.7

4.3.1.2. Skin Penetration and Mass Balance

A summary of the disposition amounts of phenanthrene are shown in Table 16. The amounts (% dose) of phenanthrene found in the skin were significantly different between 37°C and the lower (32°C) and higher (40°C) temperatures, 32.3 ± 5.2 , 15.0 ± 3.5 , and 18.3 ± 2.4 respectively. The same differences were observed in the amount of phenanthrene found in the stratum corneum. The remaining dose on the surface of the skin was significantly different at each temperature, 75.4 - 80.5% dose at 32°C, 51.5 – 63% dose at 37°C, and 70.4 – 72.8% dose at 40°C. No significant differences in the total recovery of phenanthrene was observed between temperatures.

4.3.2. Wipe Ingredient Experiments

4.3.2.1. Dermal Absorption, Flux, Lag Time, Diffusivity, and Permeability

The cumulative absorption ($\mu\text{g cm}^{-2}$) of phenanthrene when the wipe solution was generally similar to each other, however significant differences were observed between wipe 1 vs wipe 2 and wipe 2 vs wipe 3. Looking at the absorption profiles in

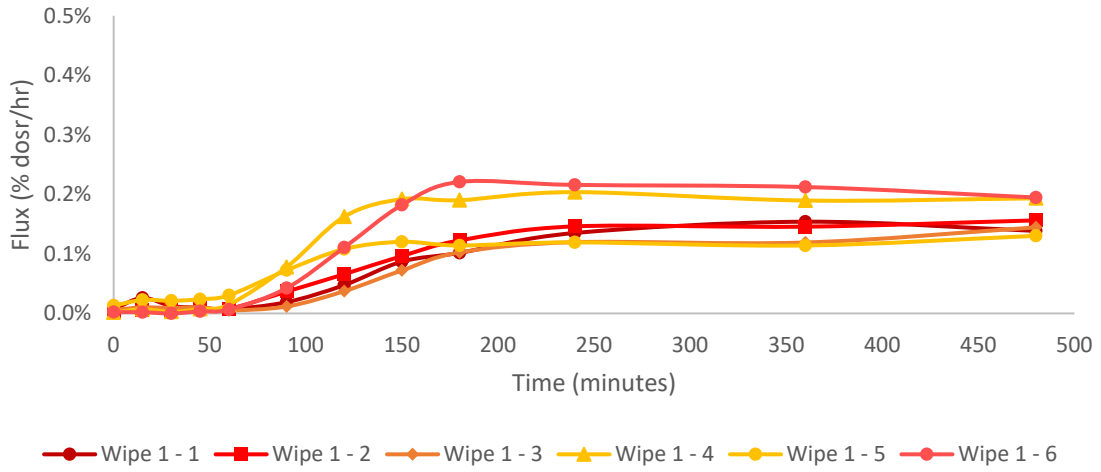
Figure 37 show wipes 1 and 3 and wipes 2 and 4 behaved very similarly. No significant differences for cumulative absorption, absorption efficiency, lag time, flux, diffusivity, or permeability were observed between wipe 1 and 3 as well as wipe 2 and 4. Although the absorption of phenanthrene was slightly different between these two groups it does suggest that differences in the wipe solution ingredients may impact dermal absorption. This is supported by the significant differences in absorption efficiency, flux, and diffusivity between wipes 1 and 2 as well as wipes 1 and 4. A summary of the absorption characteristics can be found in Table 17.

There was a noticeable decrease in the absorption of phenanthrene when the wipe solution was used, illustrated in

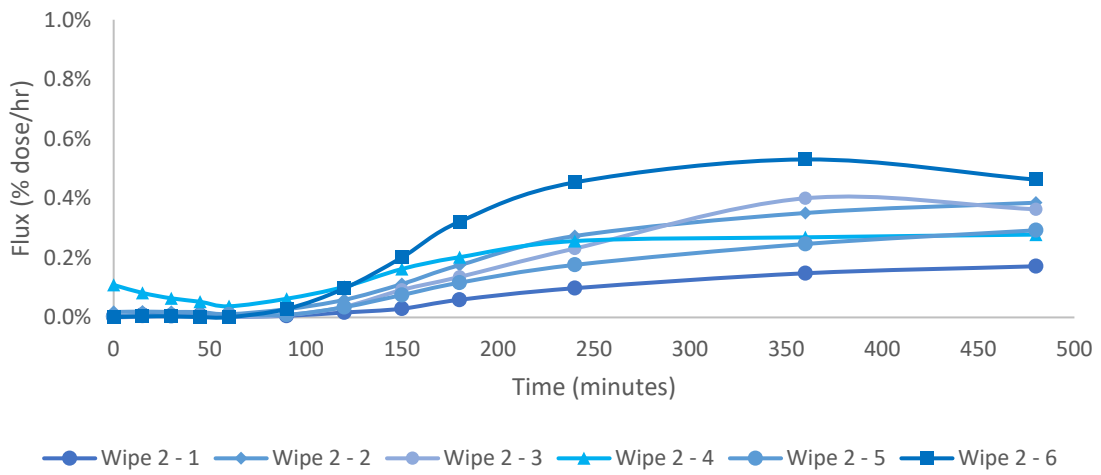
Figure 37. Overall, the absorption was lower when wipe solution was applied to the surface of the skin. However, although there were significant differences between no wipes and wipes for cumulative absorption, absorption efficiency, flux, and diffusivity, no differences were observed for permeability. Showing that the absorption differences may be more dependent on the dose.

Figure 37: Flux (% Dose/hr) profiles phenanthrene at different temperatures (A) Wipe 1, (B) Wipe 2, (C) Wipe 3, (D) Wipe 4 in an artificial sweat dosing vehicle in porcine skin in vitro. Graph E compares the flux (% Dose/hr) of all wipes to no wipe (data from Chapter 03) (error bars are standard deviation).

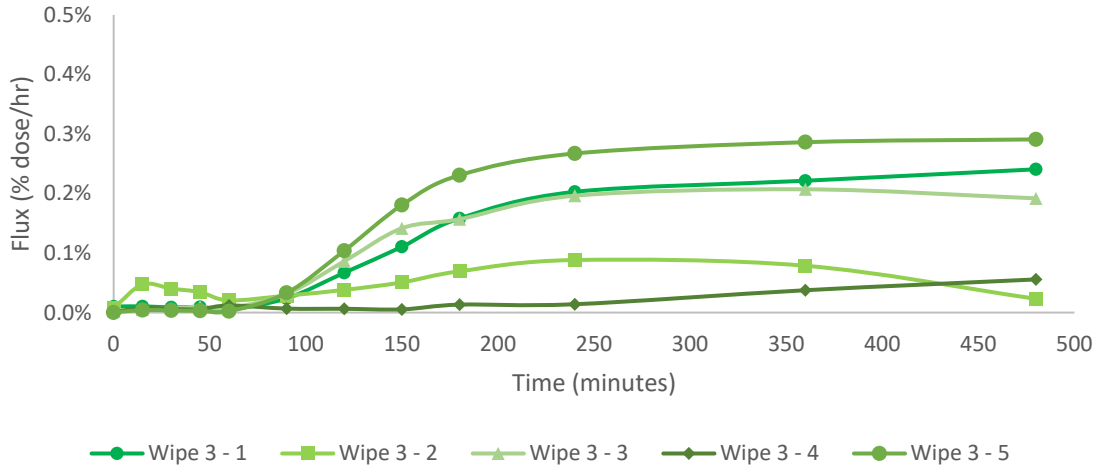
(A)



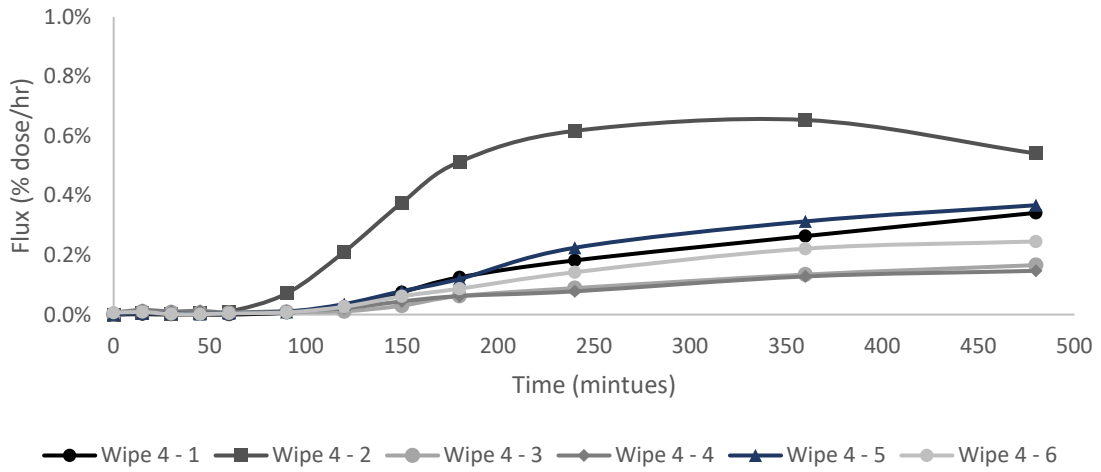
(B)



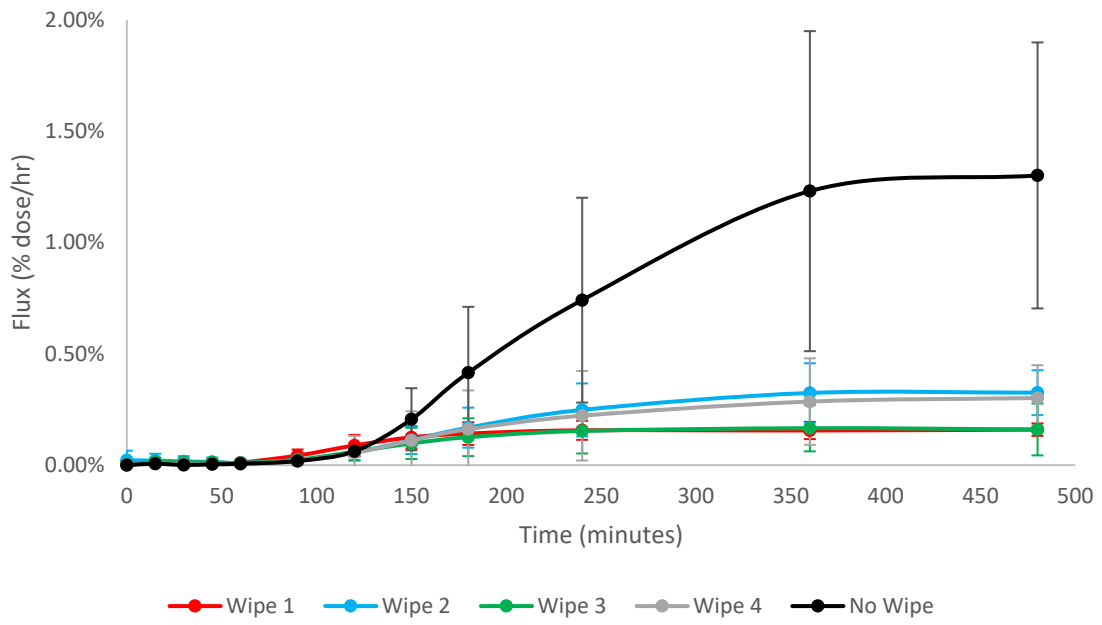
(C)



(D)



(E)



4.3.2.2. Skin Penetration and Mass Balance

Percent dose values of phenanthrene detected in the stratum corneum, skin, and skin surface are provided in Table 18. There was significantly more dose found in the stratum corneum when the wipes solution was added to the skin compared to high percent dose found in the skin when no wipes were used. The added wipe solution appears to have reduced the penetration of phenanthrene into the lower layers of the skin.

4.4. Discussion

4.4.1. Temperature Effects

The physiological effects of firefighting, such as increased skin and body temperature, increased heart rate and VO_2 max, and sweating are thought to increase dermal absorption [35, 37, 39, 41, 42, 43].

The time a firefighter can actively fight a structure fire can vary greatly due to construction, response time, resources available, cause of the fire and other factors. On average, it takes minutes to several hours to put out the average house fire. The average lag time at 37°C was 183 ± 21 which is close to three hours. Even after the temperature increase to 40°C the lag time was still greater than 2.5 hours. This suggests that there is a window of opportunity for firefighters to potentially remove chemicals from the skin and reduce their chemical exposures. However, this window of opportunity is dependent on the chemical, as seen in Chapter 03, the lag time of naphthalene was closer to 60 minutes. Furthermore, studies have shown PAH metabolites in the urine and breath after firefighter training scenarios indicating that PAHs may be absorbed through the skin within the time of fire response [218]. The exposures experienced during fire response may be difficult to prevent but the continued absorption of chemicals on the skin may be reduced by mitigation strategies such as decontamination wipes.

Table 17: Absorption characteristics of phenanthrene in porcine skin dosed with decontamination wipe ingredients applied in an artificial sweat dosing vehicle

Decontamination Wipe	Cumulative Absorption ($\mu\text{g cm}^{-2}$)	Cumulative Absorption (% Dose)	Lag Time (minutes)	Flux ($\times 10^{-2}$) ($\mu\text{g cm}^{-2} \text{hr}^{-1}$)	Diffusivity ($\times 10^{-2}$) ($\text{cm}^{-2} \text{hr}^{-1}$)	Permeability ($\times 10^{-4}$) (cm hr^{-1})
Wipe 1	0.09 ± 0.03	1.0 ± 0.3	90 ± 18	1.3 ± 0.5	63.1 ± 14.7	2.3 ± 0.8
Wipe 2	0.16 ± 0.06	1.8 ± 0.6	158 ± 33	2.9 ± 1.0	35.8 ± 6.4	5.1 ± 1.8
Wipe 3	0.09 ± 0.06	1.0 ± 0.6	131 ± 48	1.5 ± 0.9	46.2 ± 12.1	2.6 ± 1.6
Wipe 4	0.14 ± 0.09	1.6 ± 1.1	165 ± 27	2.6 ± 1.6	34.6 ± 6.3	4.5 ± 2.7
No Wipe	0.53 ± 0.25	6.8 ± 3.2	183 ± 21	10.4 ± 4.5	19.9 ± 2.2	21.0 ± 9.1

Table 18: Phenanthrene recovered from absorbed, skin, stratum corneum, and skin surface during wipe ingredients flow through experiments, as a measure of percent dose.

Decontamination Wipe	Dose ($\mu\text{g cm}^{-2}$)	Remaining Dose (% Dose)	Stratum Corneum (% Dose)	Skin (% Dose)	Absorption (% Dose)	Total Recovery (% Dose)
Wipe 1	9.0	86.8 ± 5.2	4.0 ± 4.7	2.9 ± 1.5	1.0 ± 0.3	94.6 ± 2.3
Wipe 2	9.0	81.7 ± 5.6	8.3 ± 9.5	4.0 ± 4.0	1.8 ± 0.6	95.8 ± 2.7
Wipe 3	9.0	75.9 ± 11.1	18.1 ± 14.0	4.0 ± 1.0	1.0 ± 0.6	99.0 ± 4.2
Wipe 4	9.0	82.2 ± 7.8	8.7 ± 10.2	2.8 ± 2.5	1.6 ± 1.1	95.3 ± 3.0
No Wipe	7.8	56.6 ± 3.5	2.3 ± 0.6	32.4 ± 5.2	6.8 ± 3.2	98.1 ± 3.2

There is a popular statistic used throughout the firefighting community, it states that “for every five-degree increase in temperature there is a 400% increase in skin absorption”. Unfortunately, the source of this statistic has been uncoupled from the popular “fun fact”. However, literature has shown that an increase in temperature increases dermal absorption. Blank et al. (1967) showed that the permeability constants of alcohols increase with temperature [216]. Chang and Riviere (1991) demonstrated that at increased air or perfusate temperatures absorptive flux of parathion was 2-fold greater than at standard conditions of 37°C air and 37°C perfusate. Furthermore, at high relative humidity (90%-RH) skin penetration was significantly increased at all doses [224]. Similarly, Akomeah and coworkers (2004) found a two-fold increase in flux *in vitro* after a 7 – 8°C increase (37°C to 45°C) in receptor temperature for methyl paraben and caffeine, where butyl paraben had threefold increase in flux [217].

The mechanistic effect of temperature on dermal absorption is unknown, however there are some hypotheses to explain the increased absorption at higher temperatures. One hypothesis is that at higher temperatures the barrier function of the SC decreases, as the lipids in the SC increase in fluidity. At low temperatures the SC lipids are rigid and tightly packed, and this hinders the diffusion of penetrant molecules. But at increased temperatures the lipids can more easily move, which might cause an increase in intercellular space, leading to an increase in epidermal permeability [217, 225]. Differential scanning calorimetry has shown that thermal transitions occur at skin surface temperatures near 40°, 65 – 70°C, and 80 – 85°C. However, at extreme temperatures >50°C are not applicable for *in vitro* nor *in vivo* testing nor would it be realistic for firefighters to reach said temperatures [226]. A second effect of increased temperature is the effect on the vehicle diffusion coefficient. As temperature increases some penetrating chemicals may more easily diffuse from the dosing vehicle into the skin thus increasing absorption. Another hypothesis is related to the activation energy. The activation energy is the energy level which a molecule must be raised to before it can break restraining bonds and diffuse. In general, the activation is a function of the characteristics of both the diffusion molecule and the diffusion pathway [216]. Akomeah et al. (2004) showed good linear correlation ($R^2 > 0.99$) between K_p and $1/\text{Temperature}$ for all penetrants, obtained through Arrhenius plots [217].

In this study there was a 2.4-fold increase in flux (% dose/hr) after a five degree increase from 32°C to 37°C and a 1.6-fold increase going from 37°C to 40°C. Similar increases in flux were seen in this study compared to the studies done by Akomeah and Chang. This study along with previous literature supports the idea that an increase in temperature results in an increase in dermal absorption. The differences in the rate of change may be due to vehicle effects as different vehicles were used across the studies, aqueous sweat vehicle used in this study vs organic solvent vehicles used in previous studies. Another difference is that the chemicals in the previous studies are more hydrophilic with log K_{ow} values of 3.83 parathion, -0.07 caffeine, and 1.96 methylparaben, compared to phenanthrene, which has a log K_{ow} value of 4.46.

Although there is evidence that shows at increased skin temperatures dermal absorption will be greater, there is no evidence that absorption increases by 400% as previously mentioned in the firefighter “fun fact.” This study and previous literature show that flux can increase by 60 – 140%. Additionally, the increase in absorption may be different depending on the penetrating chemical, dose vehicles, and several other environmental and skin factors. The specific experimental conditions should always be included when making a “fun fact” and should not be used as a blanket statement. It is unlikely that firefighters can prevent their core and skin temperatures from increasing, however the time firefighters operate under extreme temperatures or heavily exerting themselves should be monitored and regulated. Working in shorter bursts of action followed by regular periods of rest away from the fire would be recommended.

4.4.2. Decontamination Wipe Effects

Decontamination wipes are a relatively new mitigation strategy intended to remove chemical and particulate contamination from firefighter gear and skin. However, firefighters have expressed some concerns over the ingredients in the wipes increasing dermal absorption. These concerns are valid as various decontamination wipes include ingredients such as alcohol derivatives, skin moisturizers, and plant/oil extracts which have been shown to be potential or known penetration enhancers [227, 228, 229]. Chemical penetration enhancers increase penetration across the skin by different mechanisms of action: 1) disruption of the intercellular lipid structure between corneocytes in the SC, 2) interactions with intercellular domain of protein, 3) increasing the partitioning of a drug through solvent SC interactions, and 4) enhancers acting on desmosomal connections between corneocytes or altering metabolic activity within the skin [228].

Upon inspection of popular decontamination wipe ingredient lists there appear to be common ingredients in multiple products. These ingredients include glycerin, aloe vera extract and other plant extracts, caprylyl, tea tree oil, sodium hydroxide and sodium benzoate, polysorbate 20, and citric acid. Out of this list there are four ingredients that have been previously studied for their ability to enhance dermal absorption of drugs or chemicals: glycerin, aloe vera extract, tea tree oil, and polysorbate. Nakashima and coworkers (1996) found that glycerin significantly enhanced the absorption rate of cyclosporin three times at concentrations 6 % (v/v) dose solution [219]. Mohammadi-Samani and coworkers showed that polysorbate 80 and polysorbate 20 at different concentrations and at various mixture ratios had no detectable penetration enhancing effects on lidocaine in the guinea pig model [221]. Aloe vera gel at 0.75% dose solution (w/v) increased skin penetration of ketoprofen by 2.5 times [230]. Tea tree oil decreased skin integrity in a dose dependent manner, increasing the absorption of water by 20% in human skin at 5% of pre-treatment volume (50 $\mu\text{L}/\text{cm}^2$) [231]. Eucalyptus was shown to increase permeability coefficient of 5-fluorouracil 30 – 60-fold, but only 1.5-fold for carvedilol [232, 233, 234]. As for the other common wipe ingredients, there is little to no previous literature on their penetration enhancement effects. Further investigation would be required to test their ability to enhance dermal penetration.

This study tested four different decontamination wipe solutions containing a multitude of ingredients with an aim to investigate if the wipe solution in the decontamination wipes would increase dermal absorption. Wipe solution was applied to the skin 15 minutes after the skin was dosed with phenanthrene to mimic a firefighter using a decontamination wipe to clean their skin after exposure during a training exercise, which typically last 15 – 30 minutes. The control (no wipe) represents the absorption of a firefighter who did not use decontamination wipes.

The results in this study showed that all wipes decreased the amount of phenanthrene that was absorbed and remained in the skin. Conversely, higher amounts of phenanthrene were found in the stratum corneum compared to when no wipe was used. The lower amounts of phenanthrene found in the skin and collection media and higher amounts in the SC show that the wipe solution reduced the penetration of phenanthrene into the lower layers of the skin. The decrease in skin penetration is likely due to a dilution effect of phenanthrene on the skin. The log K_{ow} and solubility of phenanthrene is 4.46 and 1.10 mg/L in water at 25°C, respectively. These values show that phenanthrene is somewhat hydrophobic but not to a high degree. So, when the

wipe solution was added to the surface of the skin the concentration of phenanthrene on the skin would decrease and therefore decrease absorption. The importance of solubility in the dose vehicles was previously shown in Chapter 03 with the low absorption of BAP in the sweat dose vehicle.

Many creams, gels, and other solvents are frequently used as penetration enhancers, however, depending on their interaction with the penetrating chemical they may decrease absorption. This penetration reduction effect was illustrated with peppermint reducing the absorption of benzoic acid in a dose dependent manner (0.1 – 5.0% of pretreatment volume) [231]. The primary ingredient in the wipe solution is water, in general, diluted mixtures have a lower flux, approximately one tenth that of neat chemicals [207].

Among the four decontamination wipes tested two groups formed between wipes 1 and 3 and wipes 2 and 4. Albeit the differences in cumulative absorption ($\mu\text{g cm}^{-2}$) between the groups were slight there were significant differences. Even though there is a slight difference in absorption between the wipes it does suggest ingredient effect. Further examination into the minimum effective concentration for decontamination wipe ingredients may be warranted. However, even if there are some ingredients that may increase dermal absorption, they are not used at high enough concentrations to illicit a drastic effect, as seen in the comparison to no-wipe. Overall, the more toxic PAHs have higher molecular weights and more lipophilic. The results from this study would suggest that the concentration of the more lipophilic PAHs would be diluted when a decontamination wipe is used and decrease firefighters dermal absorption of these compounds.

4.5. Conclusions

No two fires are the same, meaning that firefighter exposures will be unique to the individual and to each fire. The environmental conditions, response tactics, conditions of the firefighter, and the chemicals they are exposed to will all impact an individual's exposure. The physiological responses, such as increased body and skin temperature and sweating all directly impact the condition of skin and will have subsequent impacts on dermal absorption. The results of this study further support previous literature and the fact that increased skin temperature will increase dermal absorption. Although the flux and absorption of phenanthrene increased as temperature increased the lag time of was not reduced.

On-scene decontamination may be more impactful than previously thought. Due to the long lag time of phenanthrene even at elevated temperatures suggest that contaminants may be removed from the skin with a decontamination wipe before they are absorbed into the body. Additionally, the ingredients in the decontamination wipe solution were shown to have no penetration enhancer effects, rather the contrary was observed. Firefighters should aim to limit their exposure to fire to minimize the increase in body and skin temperature. Upon exiting the fire, firefighters should wipe their skin with a wipe to remove chemicals from their skin.

The scope of this study should be expanded to test if the temperature effects are the same or greater for other PAH compounds. As shown in Chapter 03 naphthalene readily penetrates the skin and even greater amounts may be absorbed at higher temperatures, or the lag time could be reduced to the point where decontamination would be ineffective. This would be critical information in understanding the effectiveness of on-scene decontamination. In addition, benzo[a]pyrene had minimal amounts of absorption which may change at elevated temperatures.

The wipe portion of this study may also be further expanded upon. Other PAH compounds or fireground contaminants can be tested to investigate if the wipe ingredients would have a greater effect or if the dilution effect would be repeated. In this study, there was a wipe ingredient effect observed, albeit small. Further experimentation should be conducted to investigate the ingredient(s) responsible and determine the minimal effective concentration of these ingredients. This would be valuable for wipe manufacturers to include safe ingredients in their products.

4.6. Acknowledgments

This project was funded by Federal Emergency Management Agency (FEMA) with grant number EMW-2019-FP-00392-1 Effectiveness of Exposure Mitigation Strategies for Fire Investigators project via the Assistance to Firefighters Grant Program Fire Prevention and Safety (R&D) Grants.

Chapter 5: Chemical Absorption Comparison of a Synthetic Skin Model to Porcine Skin

Abstract

New firefighter mitigation strategies such as decontamination wipes have not been rigorously evaluated for their effectiveness at removing fireground contamination from the skin or gear of firefighters. One reason why decontamination wipes have not been tested is due to the lack of a standardized material that can serve as a human skin surrogate. This study aims to evaluate the chemical absorption capabilities of a synthetic skin model, SynDaver skin, at absorbing common fireground contaminants and comparing the results to porcine skin. Flow through diffusion cells were used to test the absorption of naphthalene, phenanthrene, benzo[a]pyrene, and orthophenylphenol in SynDaver skin and porcine skin. Multiple absorption parameters, such as lag time, absorption efficiency, cumulative absorption, flux, diffusivity, and permeability coefficient, were used to compare the performance of the two skin models. The SynDaver skin model was found to be less resistive to chemical absorption with higher values of cumulative absorption, absorption efficiency, flux, diffusivity, and permeability. The increased permeability of the SynDaver skin model means that it should not be used as a replacement for porcine skin or human skin for chemical absorption studies but could serve as a viable skin surrogate that may be used in the development of a wipe efficacy test method.

Keywords: Dermal Absorption, Polycyclic Aromatic Hydrocarbon, Porcine Skin, Synthetic Skin Membrane, SynDaver Skin

Highlights

- The synthetic skin model, SynDaver Skin, was shown to have comparable absorption characteristics relative to porcine skin and a strong correlation ($R^2 > 0.9$) was observed in the cumulative absorption between the two skin models.
- The synthetic skin model, SynDaver Skin, had greater absorption of all chemicals tested due to it lacking a barrier like the stratum corneum found in pigs and humans.
- The SynDaver skin model was deemed to be a suitable candidate for a human skin surrogate that may be used in the development of a wipe efficacy test method.

5.1. Introduction and Background

Several types of contaminants, including but not limited to polycyclic aromatic hydrocarbons (PAHs), flame retardants, volatile organic compounds, and heavy metals have been found on the fireground, gear, and skin of firefighters [24, 53, 65, 173, 174, 200]. Furthermore, exposures to some of these chemicals have been found to exceed either published ceiling values, short-term exposure limits, or NIOSH recommended exposure limits in air [24, 94]. The chemicals that encounter skin through direct deposition or handling dirty gear may penetrate the skin and contribute to the dermal exposure firefighters experience while on the fireground [195].

Decontamination strategies, such as decontamination wipes, have been implemented to remove contaminants from firefighter skin. Unfortunately, there is no standardized test method for evaluating decontamination wipe effectiveness at removing contaminants from human skin, primarily due to the lack of a human skin surrogate that can be used to simulate dermal absorption after fireground exposures in the laboratory. Fortunately, there are several synthetic skin models that may be viable for this application.

Numerous experiments have been conducted on a wide range of chemicals to understand dermal absorption in human skin and other skin models. While human skin would be most appropriate for chemical dermal absorption testing, it is often difficult to obtain, therefore animal and synthetic skin models are used as preliminary screening tools [203, 208, 235]. Several animal species have been compared to human skin but due to differences in skin morphology and hair density many animal species fail to replicate the same behaviors of human skin, except for one species, pigs [114, 202, 204]. Porcine skin is most analogous to human skin because of its similar stratum corneum structure and skin morphology to human skin [153]. For most compounds tested, porcine skin was similar to human skin absorption ranging 50 – 150% [153, 207]. Other animals like rodents (rats or mice), rabbits, and guinea pigs have been used in dermatotoxicological studies and have had absorption rates significantly higher compared to human skin, sometimes 40 to 1600 times more permeable than human skin [102, 153]. Therefore, these animal models are primarily used as preliminary evaluations of a chemical's ability to penetrate skin.

Dermal absorption studies have shown that synthetic skin models could be more advantageous for screening applications than animal skin models because of their low cost, ease of storage, and better control over physical properties, while also avoiding any ethical concerns

typically associated with animal or human experiments. Several synthetic materials have been used to model the sweating, surface properties, mechanical properties, acoustic properties, optical properties, and thermal properties of human skin [156].

Polymer skin models, polydimethylsiloxane (PDMS) specifically, are popular synthetic skin models that have been compared to human and porcine skin models using hydrophilic and lipophilic compounds [157, 159, 160, 210]. Uchida et al. (2016) tested several chemicals in a silicone membrane, hairless rat skin, and human skin and found that the permeation coefficient of hydrophilic compounds were similar in all skin models, for amphiphilic compounds the silicone model was 10 times higher than in the hairless rat and human skin, and for lipophilic compounds the permeation coefficient values were 100 times higher in the silicone membrane than in hairless rat and human skin [157]. Other synthetic skin models are designed to mimic the layered morphology of human skin, Strat-M® transdermal diffusion membrane is one such example. The membrane is a multilayered structure with a tight top layer to resemble the stratum corneum, underneath are two layers of polyethersulfone to resemble the dermis of human skin, and polyolefin non-woven fabric support to resemble the subcutaneous tissue in human skin [158]. Polyurethanes have also been utilized as human skin surrogates for mechanical property testing because their properties can be easily manipulated by changing the ratio of monomers and additives [156].

Out of the several synthetic skin models currently available, the synthetic skin model selected for chemical absorption comparison to porcine skin for potential later use in a wipe efficacy test method was SynDaver Skin. The SynDaver tissue plate is a product designed to simulate the mechanical properties of skin and has been used for training intradermal injections and skin surgeries in the medical field [236]. There are few to no studies comparing the permeation between SynDaver tissue plates and human skin. However, mechanical and deformation behavior comparisons have been made, where the SynDaver tissue plate was found to undergo less deformation under equivalent loads compared to human skin and decreased in friction under wet conditions compared to human skin [161]. Other synthetic skin models have been developed, such as Strat-M membrane, however, models like Strat-M membrane lack the physical properties that would be beneficial in a wipe test. Having comparable mechanical and physical properties are crucial for a synthetic skin model to be considered for use in a wipe

efficacy test method. Therefore, the SynDaver tissue plate skin model was selected for chemical absorption comparison to porcine skin.

This research is aimed at identifying a synthetic skin model that may serve as a human skin surrogate to develop a standardized wipe test method. Previous decontamination wipe studies have used non-porous materials as their skin models which are incapable of replicating the barrier function and absorptive properties of human skin [183, 184, 185]. Furthermore, the use of these types of materials may falsely inflate the effectiveness of the wipe tested because the contaminants are unable to penetrate the material and stay on the surface. The synthetic skin model that has been selected for chemical absorption studies has been shown to have comparable mechanical and physical properties to human skin. The physical properties are important to consider because the simulation of the resistive and frictional forces that occur during wiping are necessary to predict a wiper's performance in the field. The chemical properties are vital to accurately predict a wipe's ability to remove contaminants from skin. This study will compare the chemical absorption properties of a synthetic skin model to porcine skin, the most similar animal skin model to human skin, using a flow through diffusion cell system and three PAH compounds and one known skin penetrant. Comparisons of multiple absorption parameters lag time, flux, cumulative absorption, and permeability will provide context on whether SynDaver skin is a viable material that could be used as a human skin surrogate in the development of a standardized wipe test method.

5.2. Methodology and Materials

5.2.1. Chemicals

Test chemicals ^{14}C -naphthalene (specific activity = 57 mCi/mmoL), ^{14}C -phenanthrene (specific activity = 55 mCi/mmoL), ^{14}C -benzo[a]pyrene (specific activity = 26.6 mCi/mmoL), and ^{14}C -orthophenylphenol (specific activity = 150 mCi/mmoL) were obtained from American Radiolabeled Chemicals (Saint Louis, MO, USA). Chemical properties of the radiolabeled chemicals can be seen in Table 19. Artificial eccrine perspiration (pH=4.5 stabilized with bactericide and fungicide), an artificial sweat, was used as the dosing vehicle and obtained from Pickering Laboratories (USA). The cells used for the flow through experiment were 9mm (0.64 cm²) in-line diffusion cells obtained from PermeGear (USA). The collection media was made up the day before the experiment and frozen overnight. Ingredients for the collection media included: bovine serum albumin fraction V (2.25% w/v), sodium chloride (0.3% w/v), potassium

chloride (0.018% w/v), calcium chloride (0.014% w/v), potassium phosphate monobasic (0.008% w/v), magnesium sulfate (0.015% w/v), sodium bicarbonate (0.14% w/v), dextrose (0.06% w/v), distilled water (96.94% v/v), sodium heparin (0.25% v/v), amikacin (0.0063% v/v), and penicillin G sodium (0.0025% v/v) (Millipore Sigma, USA).

Table 19: Chemical properties of ^{14}C radiolabeled compounds used in flow through experiments

Compound	Naphthalene	Phenanthrene	Benzo[a]pyrene	Orthophenylphenol
Formula	C_{10}H_8	$\text{C}_{14}\text{H}_{10}$	$\text{C}_{20}\text{H}_{12}$	$\text{C}_{12}\text{H}_{10}\text{O}$
Cas Number	91-20-3	85-01-8	50-32-8	90-43-7
Molecular Weight	128.2	178.2	252.3	170.21
# of Aromatic Rings	2	3	5	2
Specific Activity (mCi/mmol)	57	55	27	150
Concentration (mCi/mL)	0.1	0.1	0.1	0.1
Solvent	Ethanol	Ethanol	Toluene	Ethanol
Log Kow	3.30	4.46	6.13	3.09
Solubility in Water at 25°C (mg/L)	31	1.10	0.00162	0.70
Radioactivity	1 - ^{14}C	9 - ^{14}C	7 - ^{14}C	Ring - ^{14}C

5.2.2. Flow Through Diffusion Cell Set Up

The flow through diffusion cell system, described by Bronaugh and Stewart [205], was used to perfuse porcine skin and synthetic skin (SynDaver skin) membranes. Fresh porcine skin was obtained from Yorkshire/Landrace pigs (20 – 60 kg). The pigs were shaved and dermatomed to a thickness of 200-300 μm with an electric dermatome (Padgett Instruments, Kansas City, MO, USA). Afterwards, each piece of skin was cut into a circular disk, placed into the diffusion cell, and secured in place, providing a dosing surface area of 0.64 cm^2 . The porcine skin membranes were dosed within 30 minutes of death of the porcine skin donor, so skin integrity testing was not necessary [206].

The underside of the skin disks was perfused with a bovine serum albumin collection media and maintained at a pH between 7.3 and 7.6. The temperature of the perfusate and diffusion cells were maintained at $37^{\circ}\text{C} \pm 1^{\circ}\text{C}$ using a heating block. The flow rate was maintained at 4 mL h^{-1} using a peristaltic pump. The room temperature and relative humidity were recorded throughout the experiment for record keeping. Perfusate samples were collected in glass scintillation vials at times: 0, 15, 30, 45, 60, 75, 90, 120, 180, 240, 360, and 480 minutes. After the flow-through diffusion cell systems were set up the chemical doses were added to each cell. The time for the experiment and sample collection started immediately after the last cell was dosed.

5.2.3. Dosing Procedure

Test chemicals ^{14}C -naphthalene, ^{14}C -phenanthrene, ^{14}C -benzo[a]pyrene, and ^{14}C -orthophenylphenol were made into separate dose mixtures. Each dosing solution was prepared by adding the test chemical to artificial sweat and then adding acetone (1% of total volume). Each dosing solution was vortexed to ensure the test compound was thoroughly mixed. Skin disks were dosed with 100 μL of the respective dosing solution administered through a delivery channel to the top of the cell. Applying either $1.6 \mu\text{g}/\text{cm}^2$ (0.5 μCi) of NAP (n=5), $7.8 \mu\text{g}/\text{cm}^2$ (1.5 μCi) of PHEN (n=3), $36.0 \mu\text{g}/\text{cm}^2$ (2.5 μCi) of BAP (n=6), and $2.0 \mu\text{g}/\text{cm}^2$ (1.1 μCi) of OPP (n=7). After dosing, diffusion cells were covered with Parafilm® pieces (Pechiney Plastic Packaging, IL, USA) to minimize the loss of semi-volatile compounds.

5.2.4. Sample Analysis

Perfusate samples were taken at time points: 0, 15, 30, 45, 60, 75, 90, 120, 180, 240, 360, and 480 minutes after dosing. After the experiment, aliquots of the perfusate were transferred to new scintillation vials along with 15 mL of BioScint (National Diagnostics, GA, USA) and analyzed using a liquid scintillation counter for ^{14}C determination. At the end of the experiment the remaining dose was removed from the surface of the skin membrane with a cotton swab. The skin membranes were transferred to wax paper, where the surface of each skin disk was then tape-stripped (Scotch Tape; 3M, St. Paul, MN, USA) six times, placing three strips into a single scintillation vial, and adding 10 mL of ethyl acetate. After tape-stripping the center of the skin disks were punched with an 8mm biopsy tool, the center and peripheral skin were separated and placed into individual scintillation vials along with 2 mL of BioSol. The skin samples were incubated at 50°C for 8 – 12 hours and analyzed using a liquid scintillation counter for ^{14}C

determination. The fingertips of the gloves used during swabbing and tape stripping were extracted with ethanol.

5.2.5. Absorption Calculations

Absorption was defined as the total percentage of dose detected in the perfusate. Cumulative absorption ($\mu\text{g cm}^{-2}$) was calculated by summing the total dose that was detected in the perfusate at each sampling time. Flux ($\mu\text{g cm}^{-2} \text{hr}^{-1}$) was obtained from the steady-state slope of the cumulative absorption versus time curves. The permeability coefficient (K_p) (cm hr^{-1}) was calculated from the ratio of the flux ($\mu\text{g cm}^{-2} \text{hr}^{-1}$) to the concentration (C_s) ($\mu\text{g cm}^{-3}$) of the dose. The dose concentration was obtained from 10- μL pre- and post-dose checks. The lag time (τ) was obtained by extrapolated the steady-state portion of the curve back to the time- or x-axis. This lag time was related back to diffusivity (D) and membrane thickness (L) by the following equation: $D=L^2/6(\tau)$. Student's t-test was performed to determine significant differences at $P < 0.05$. The data presented in this chapter were compared to the chemical absorption data in CHAPTER 3. The flux, diffusivity, permeability coefficient, cumulative absorption ($\mu\text{g}/\text{cm}^2$ and percent dose), and mass balance were compared to determine if the SynDaver skin model is capable of absorbing PAHs similar to porcine skin. Statistical tests were performed for several absorption characteristics between the skin models for each of the compounds tested. Statistical tests with results are listed in Table 20.

Table 20: Test for statistical difference using student-t tests ($p < 0.05$) for absorption characteristics of PAH compounds and OPP in porcine skin and SynDaver skin using an artificial sweat dosing vehicle

Compound	NAP	PHEN	BAP	OPP
Comparison	PIG vs SynDaver	PIG vs SynDaver	PIG vs SynDaver	PIG vs SynDaver
Statistical Test	Student T-Test	Student T-Test	Student T-Test	Student T-Test
Flux (% Dose/hr)	YES	YES	YES	YES
Flux ($\mu\text{g}/\text{cm}^2/\text{hr}$)	YES	YES	YES	YES
Cumulative Absorption ($\mu\text{g}/\text{cm}^2$)	YES	YES	YES	YES
Absorption Efficiency (% Dose)	YES	YES	YES	YES
Diffusivity (cm^2/hr)	YES	YES	YES	YES
Permeability (cm/hr)	YES	YES	YES	YES
Lag Time (minutes)	YES	YES	YES	YES

5.3. Results and Discussion

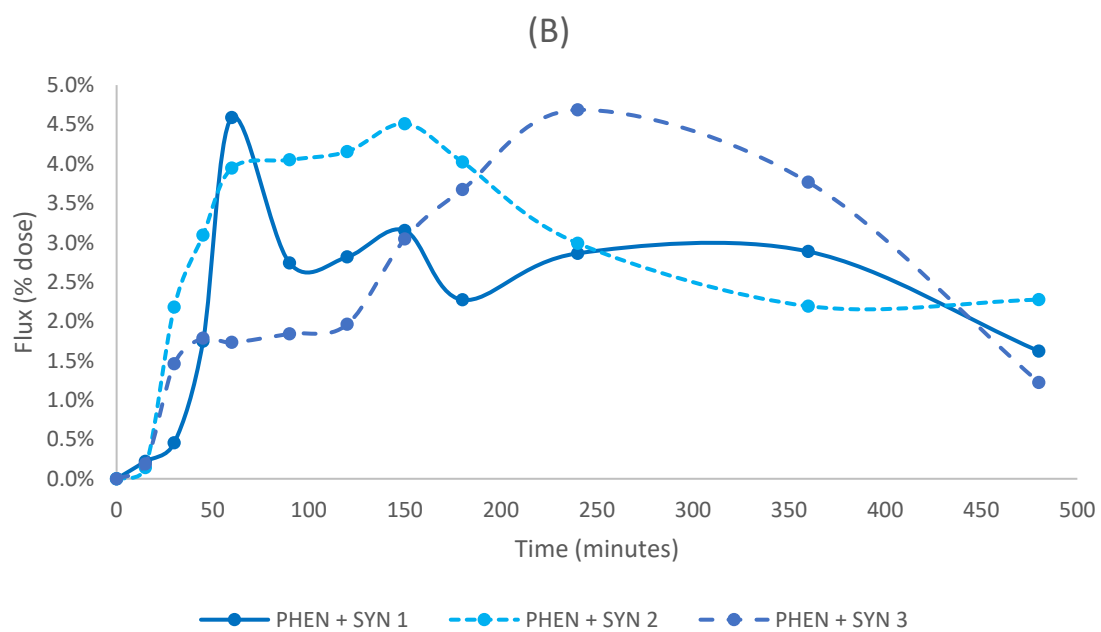
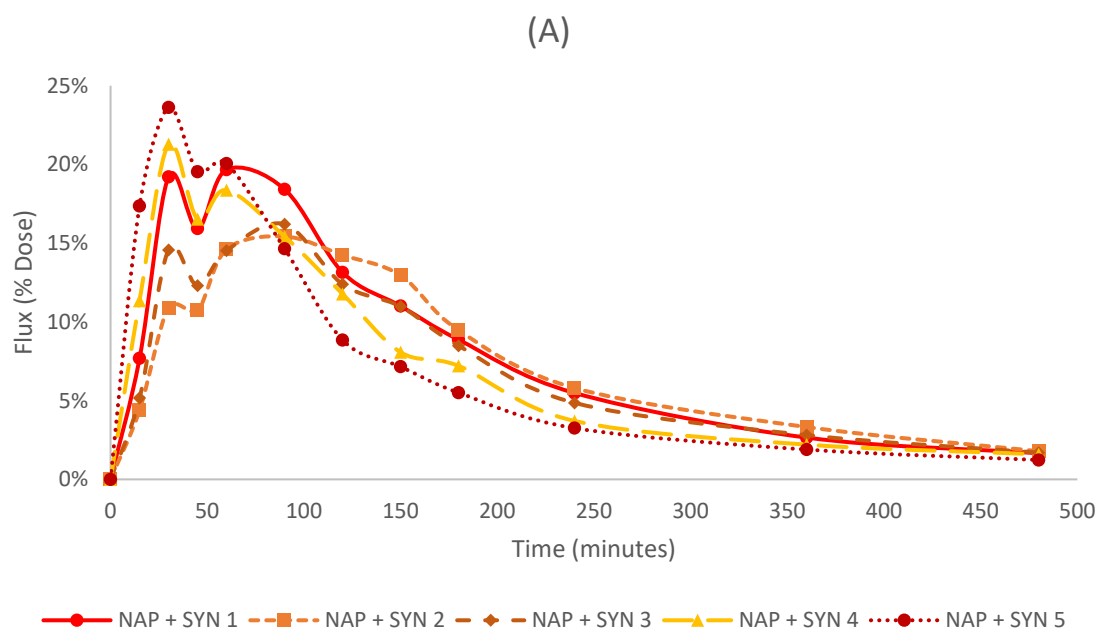
5.3.1. Absorption, Flux, Diffusivity, and Permeability

The flux (% dose/hr) of the three PAH compounds tested, shown in Figure 38, were influenced by the molecular weight of the compound. The smallest MW PAH studied, naphthalene, had the greatest max flux (15 – 24% dose/hr) followed by the middle MW PAH, phenanthrene, with a max flux of (3 – 5% dose/hr), and the largest MW PAH compound, benzo[a]pyrene, was the lowest max flux of the PAH compounds (0.01 – 0.03% dose/hr). Orthophenylphenol has a molecular weight in between naphthalene and phenanthrene but its log K_{ow} value is lower than naphthalene so its flux (8 – 19% dose/hr) ranked in between the two PAH compounds. The rank of the flux for the compounds tested follow the 500 Dalton rule, which states that as the molecular weight of a chemical increases absorption is less likely to occur [137].

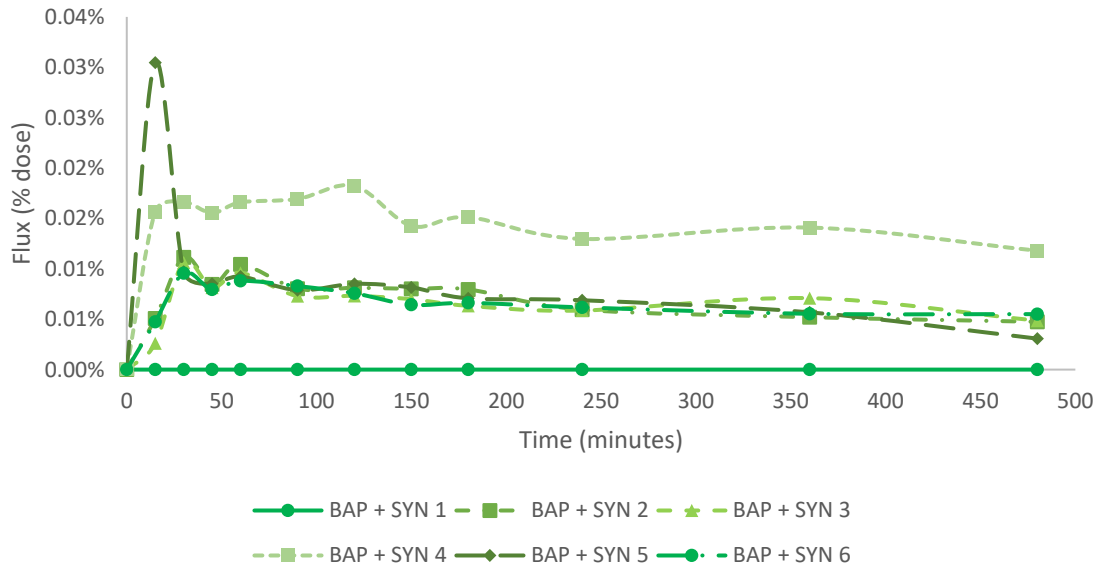
The order of absorption efficiency for the PAH compounds was the same, naphthalene ($51 \pm 3\%$ dose) having the greatest cumulative percent dose absorbed, followed by phenanthrene ($21 \pm 2\%$ dose), and benzo[a]pyrene ($0.048 \pm 0.003\%$ dose) was lowest. The absorption efficiency of orthophenylphenol ($52 \pm 5\%$ dose) was similar to that of naphthalene. The cumulative absorption ($\mu\text{g cm}^{-2}$) of naphthalene, phenanthrene, benzo[a]pyrene, and orthophenylphenol were 0.80 ± 0.05 , 1.61 ± 0.13 , 0.017 ± 0.001 , and 0.96 ± 0.07 , respectively. The absorption profiles of the chemicals are shown in Figure 39 and Figure 40. Although naphthalene and orthophenylphenol had greater absorption efficiencies than phenanthrene, phenanthrene had greater cumulative absorption. This is due to the differences in molecular weight and dose, which greatly impact cumulative absorption. The diffusion cells were intended to be dosed with $1.0 - 1.5 \mu\text{Ci/cell}$ to limit the amount of radioactivity used for the experiment. If all cells were dosed with the same amount of radioactivity (μCi), the mass of each compound would be different due to their differences in molecular weight; PHEN is 178.23 g/mol , NAP 128.17 g/mol , and OPP 170.21 g/mol . Furthermore, the volatile nature of NAP resulted in approximately half the intended dose being delivered to the skin.

The lag time of all chemicals was relatively fast in the SynDaver skin model. All compounds reached steady state in under an hour, naphthalene 9 ± 6 minutes, phenanthrene 50 ± 24 minutes, and orthophenylphenol 17 ± 9 minutes. However, due to the low absorption of benzo[a]pyrene and test duration it was likely that steady state was never reached, and subsequent calculations of lag time, diffusivity, and permeability coefficient would have low confidence in their accuracy and were therefore not calculated. The flux ($\mu\text{g cm}^{-2} \text{ hr}^{-1}$) of naphthalene, phenanthrene, and orthophenylphenol were 0.27 ± 0.04 , 0.29 ± 0.05 , and 0.20 ± 0.05 , respectively. The diffusivity ($\text{cm}^2 \text{ hr}^{-1}$) of naphthalene, phenanthrene, and orthophenylphenol were 8.1 ± 8.2 , 0.8 ± 0.3 , 2.9 ± 1.9 , respectively. The permeability coefficient ($\times 10^{-3}$) of naphthalene, phenanthrene, and orthophenylphenol was 27.1 ± 4.3 , 5.9 ± 1.1 , and $17.0 \pm 4.9 \text{ cm/hr}$, respectively. No significant differences in flux or diffusivity were observed between naphthalene, phenanthrene, or orthophenylphenol, but for the permeability coefficient, significant differences were observed between phenanthrene vs naphthalene ($p < 0.05$) and phenanthrene vs orthophenylphenol ($p < 0.05$).

Figure 38: Flux (% Dose/hr) versus time (hr) plot for (a) naphthalene, (b) phenanthrene, (c) benzo[a]pyrene, and (d) orthophenylphenol in artificial sweat following topical application to SynDaver skin in vitro flow through diffusion cell.



(C)



(D)

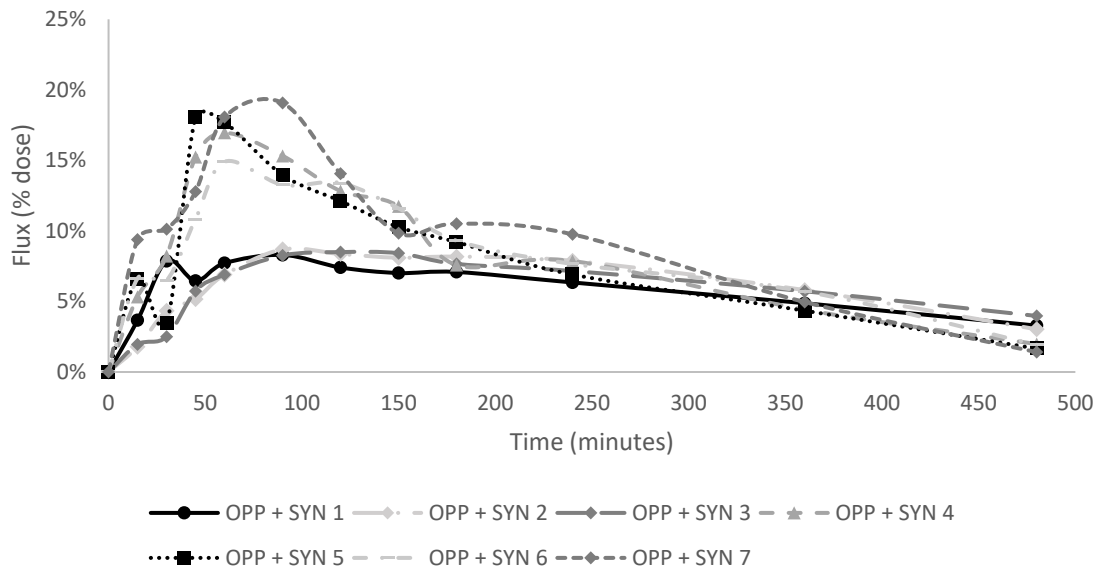
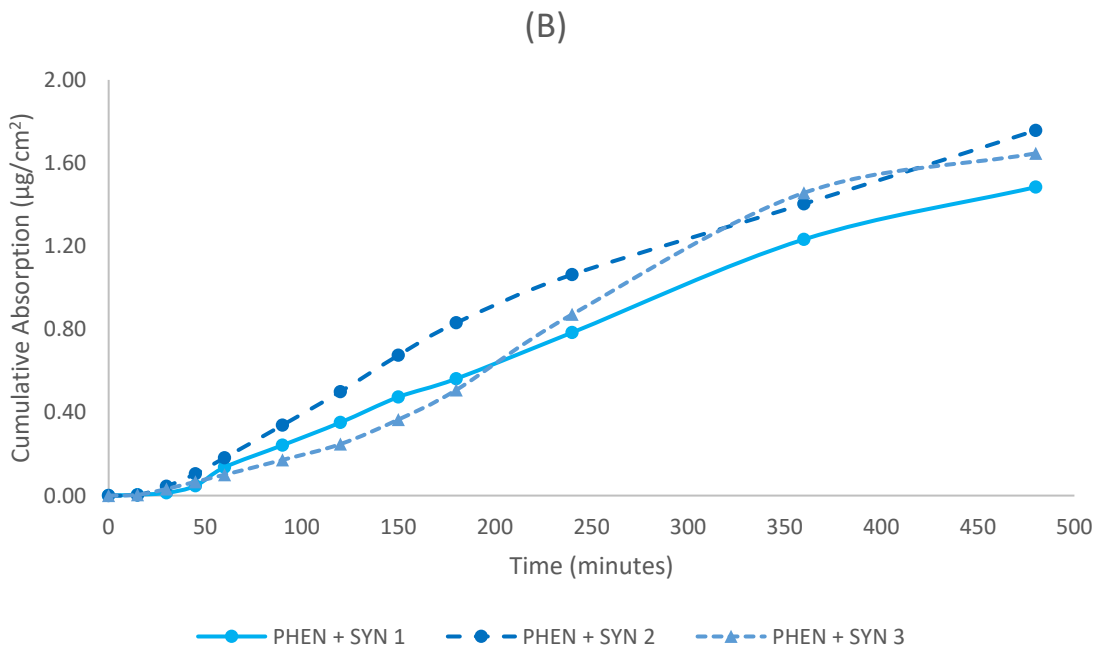
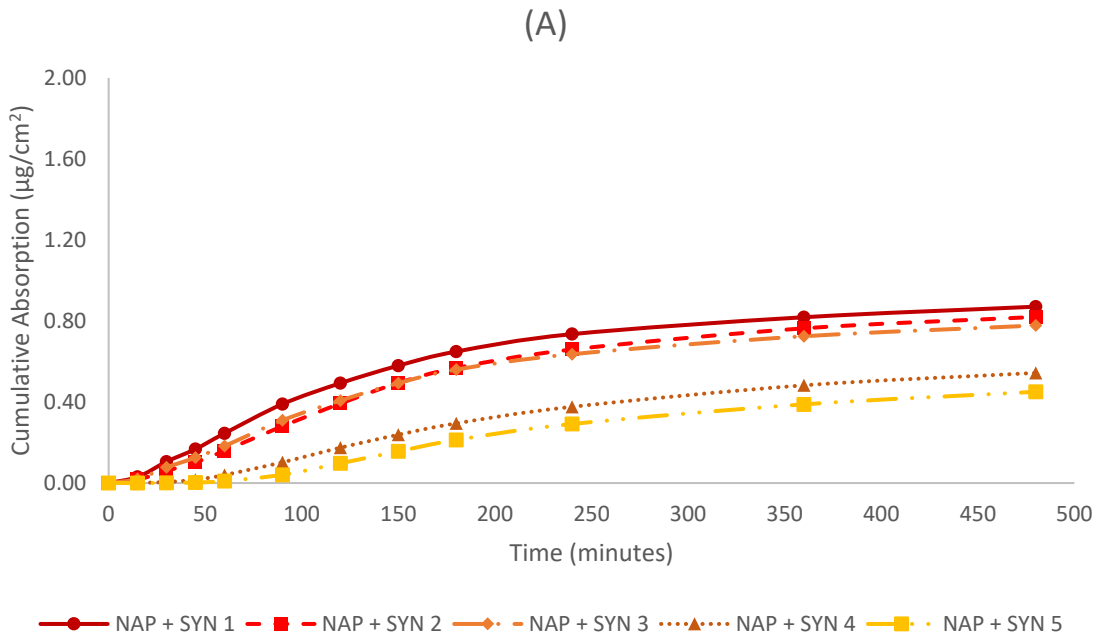
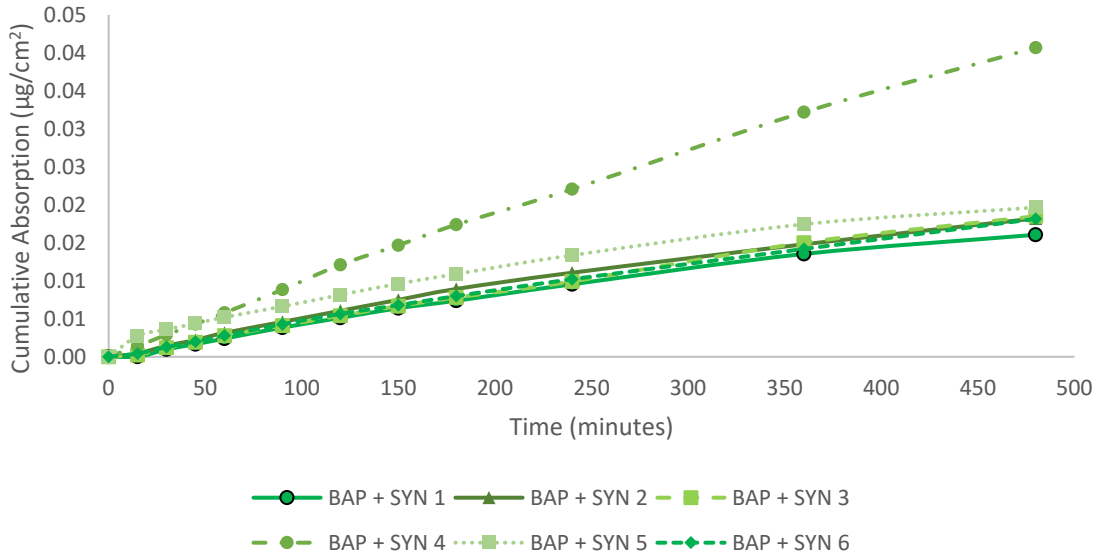


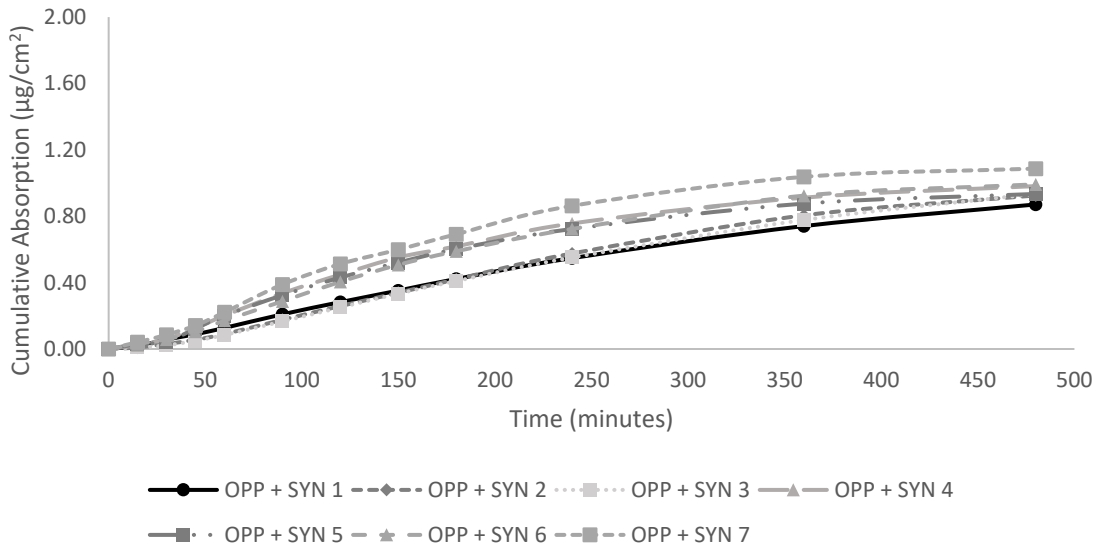
Figure 39: Cumulative Absorption ($\mu\text{g cm}^{-2}$) versus time (minutes) for (A) naphthalene, (B) phenanthrene, (C) benzo[a]pyrene, and (D) orthophenylphenol in artificial sweat following topical application to SynDaver skin in vitro flow through diffusion cell.



(C)



(D)



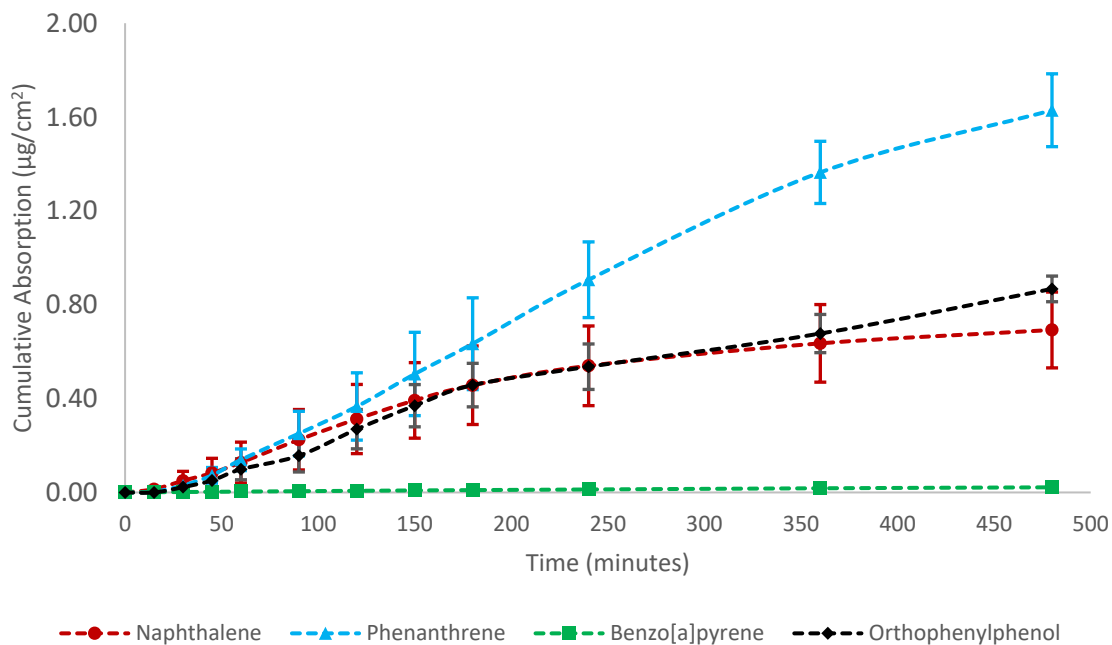


Figure 40: Cumulative absorption (% dose) versus time (hr) plot for naphthalene, phenanthrene, benzo[a]pyrene, and orthophenylphenol in SynDaver skin (error bars are standard deviation)

5.3.2. SynDaver Skin vs Porcine Skin Comparison

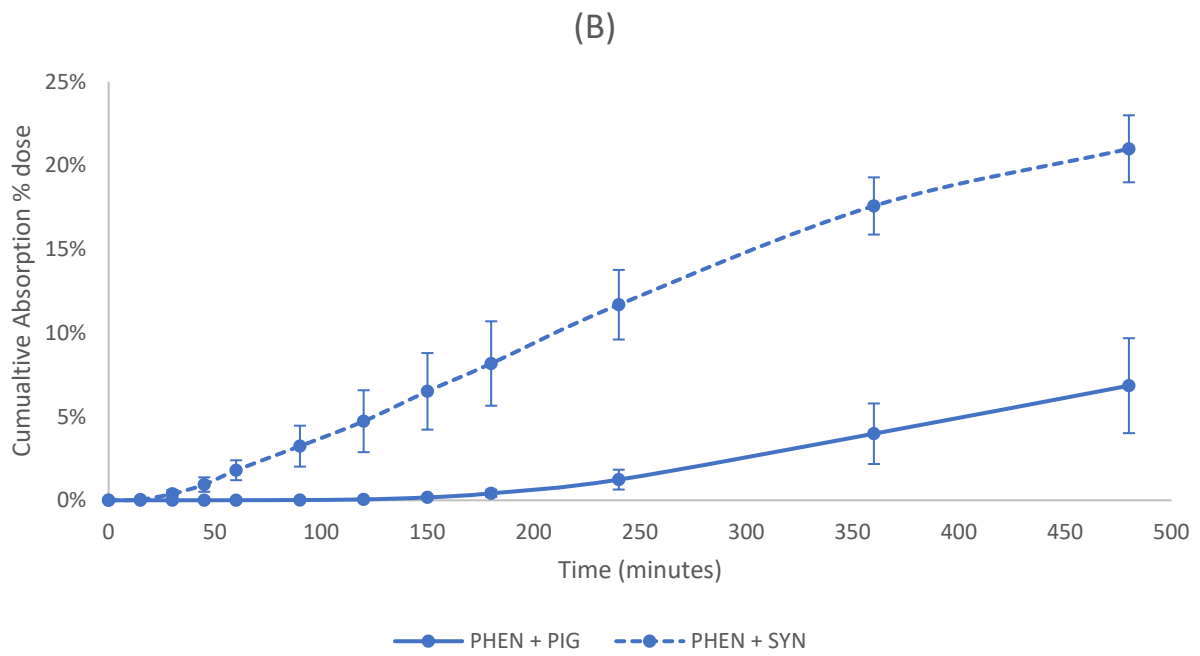
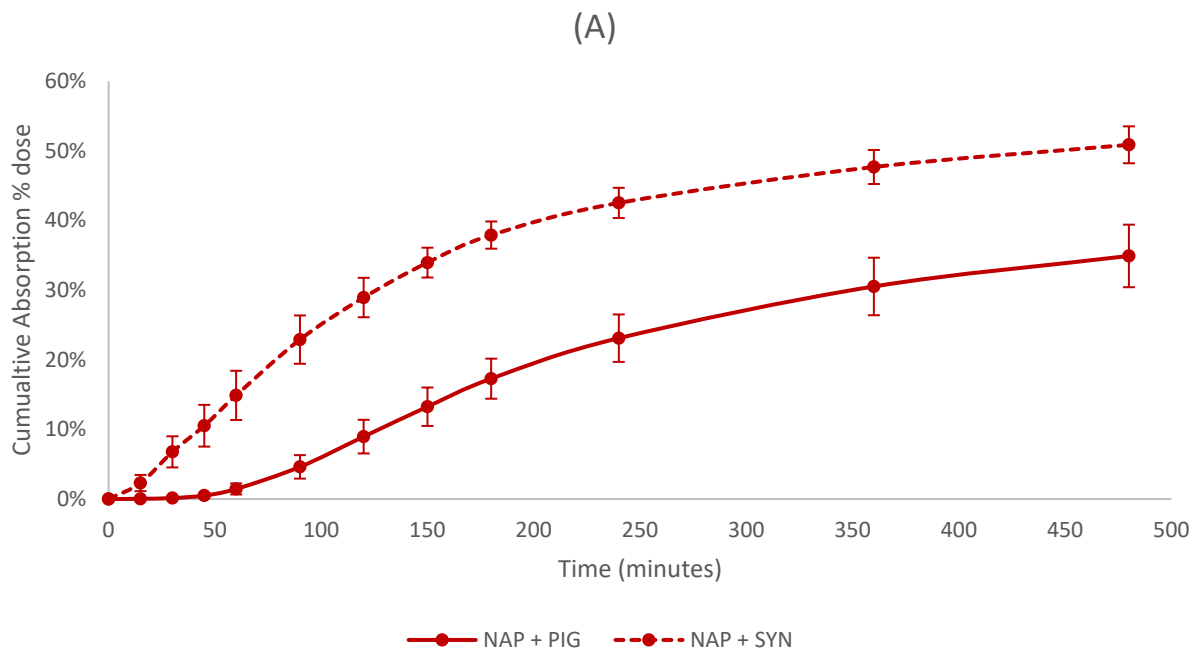
During the porcine flow through experiments, discussed in CHAPTER 03, there were also minimal amounts of benzo[a]pyrene was able to penetrate the skin (<1% dose) which lead to decreased confidence in subsequent absorption characteristic calculations. The low absorption was again observed in the SynDaver skin model. The repeated low absorption of benzo[a]pyrene in both skin models appears to be due to the low solubility of benzo[a]pyrene in the artificial sweat dosing vehicle and not an issue with the skin models. The low solubility would result in benzo[a]pyrene having little mobility in the vehicle and never contacting either skin membrane, resulting in low absorption. Due to the low absorption of benzo[a]pyrene in both skin models, no comparisons between porcine skin and SynDaver skin will be made. Comparisons between the SynDaver skin model and porcine skin model will focus on naphthalene, phenanthrene, and orthophenylphenol.

The flux ($\mu\text{g cm}^{-2} \text{hr}^{-1}$) of naphthalene, phenanthrene, and orthophenylphenol were all higher in the SynDaver skin model, ranging 2.3 – 2.7 times greater than the flux reported in the porcine skin model. Greater cumulative absorption ($\mu\text{g cm}^{-2}$) and absorption efficiency (% dose) were

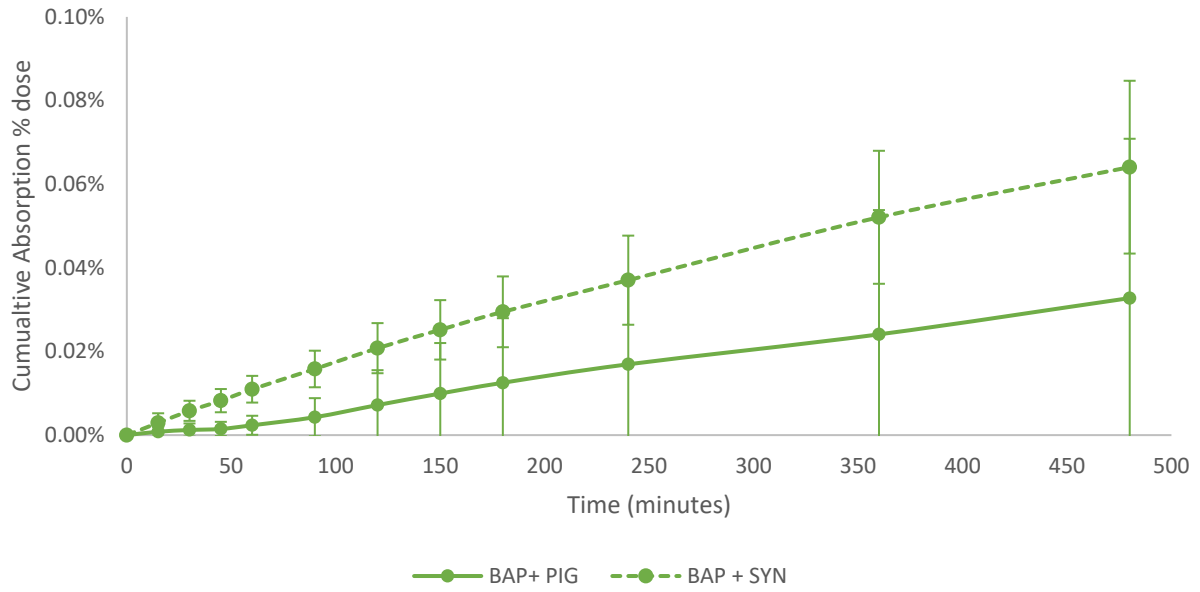
also greater in the SynDaver skin model than in the porcine skin model, ranging 1.4 – 3.1 times higher. The absorption profiles of NAP, PHEN, BAP, and OPP in porcine skin and SynDaver skin is shown in

Figure 41 and demonstrates the greater absorption in the synthetic skin model. The time for the compounds to reach steady state was drastically shorter, 47 – 85% faster, in the SynDaver skin. Similarly, the values of diffusivity and permeability coefficient were greater in the SynDaver skin model, 3.9 – 10.0 times higher and 2.2 – 2.8 times higher, respectively. A summary table of the absorption parameters and mass balance for all chemicals tested in both skin models can be found in Table 21 and Table 22, respectively.

Figure 41: Absorption profiles (cumulative absorption % dose) of (A) NAP, (B) PHEN, (C) BAP, and (D) OPP in porcine skin and SynDaver skin in an artificial sweat dosing vehicle. (error bars are standard deviation)



(C)



(D)

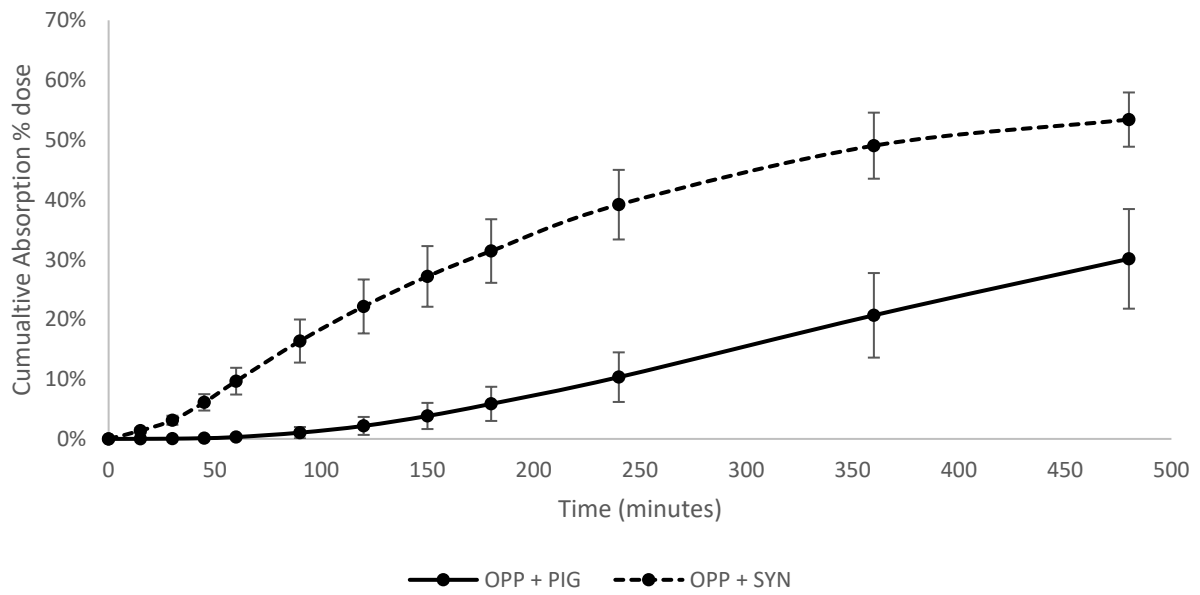


Table 21: Summary Table of the Absorption Parameters of the ¹⁴C Compounds in Porcine skin and SynDaver Skin

Porcine Skin	Naphthalene	Phenanthrene	Benzo[a]pyrene	Orthophenylphenol
Lag Time (minutes)	52 ± 8	183 ± 21	N/A*	103 ± 18
Flux (×10⁻²) (µg cm⁻² hr⁻¹)	12.1 ± 1.7	10.4 ± 4.5	N/A*	8.5 ± 2.4
Diffusivity (×10⁻²) (cm² hr⁻¹)	81.2 ± 2.3	19.9 ± 2.2	N/A*	42.2 ± 8.5
Permeability (cm hr⁻¹)	0.012 ± 0.001	0.002 ± 0.001	N/A*	0.007 ± 0.002
Permeability (×10⁻³) (cm hr⁻¹)	12.0 ± 1.7	2.1 ± 0.9	N/A*	7.3 ± 2.4
SynDaver Skin	Naphthalene	Phenanthrene	Benzo[a]pyrene	Orthophenylphenol
Lag Time (minutes)	9 ± 6	50 ± 24	N/A*	17 ± 9
Flux (×10⁻²) (µg cm⁻² hr⁻¹)	27.3 ± 4.3	29.3 ± 5.5	N/A*	19.9 ± 4.7
Diffusivity (×10⁻²) (cm² hr⁻¹)	814.7 ± 811.8	78.4 ± 27.6	N/A*	288.1 ± 193.5
Permeability (cm hr⁻¹)	0.027 ± 0.004	0.006 ± 0.001	N/A*	0.017 ± 0.005
Permeability (×10⁻³) (cm hr⁻¹)	27.1 ± 4.3	5.9 ± 1.1	N/A*	17.0 ± 4.9
*Values are not provided due to absorption likely not reaching steady state thus reducing the confidence of subsequent calculations with the absorption parameters.				

Table 22: Mass Balance of ^{14}C Compounds in porcine skin and SynDaver skin from an artificial sweat dose vehicle

Porcine Skin	Naphthalene	Phenanthrene	Benzo[a]pyrene	Orthophenylphenol
Dose ($\mu\text{g cm}^{-2}$)	1.6	7.8	36.0	2.0
Swab (% Dose)	60.3 \pm 4.5	56.5 \pm 3.5	98.1 \pm 1.8	56.4 \pm 11.7
Stratum Corneum (% Dose)	0.1 \pm 0.1	2.3 \pm 0.6	0.1 \pm 0.1	0.3 \pm 0.4
Skin (% Dose)	0.7 \pm 0.2	32.4 \pm 5.2	1.6 \pm 1.7	10.6 \pm 3.3
Absorption (% Dose)	35.0 \pm 4.6	6.8 \pm 3.2	0.1 \pm 0.1	30.1 \pm 9.5
Total Recovery (% Dose)	96.1 \pm 1.1	98.1 \pm 3.3	99.9 \pm 1.9	97.4 \pm 3.0
SynDaver Skin				
Dose ($\mu\text{g cm}^{-2}$)	1.6	7.8	36.0	2.0
Swab (% Dose)	48.4 \pm 3.9	75.7 \pm 1.7	98.6 \pm 1.2	43.2 \pm 6.5
Stratum Corneum (% Dose)	0.3 \pm 0.1	0.1 \pm 0.0	0.0 \pm 0.0	0.1 \pm 0.1
Skin (% Dose)	0.1 \pm 0.1	0.7 \pm 0.4	0.0 \pm 0.0	2.7 \pm 2.4
Absorption (% Dose)	50.8 \pm 3.0	20.7 \pm 1.7	0.0 \pm 0.0	52.2 \pm 6.4
Total Recovery (% Dose)	99.6 \pm 2.1	97.2 \pm 3.6	98.7 \pm 1.2	98.2 \pm 2.1

Unlike biological skin models like porcine skin, SynDaver skin lacks a superficial barrier analogous to the stratum corneum, metabolic capability, and organizational structure of cells and lipids. Minimal amounts (< 1% dose) of NAP, PHEN, and OPP were found in the tape strips, which typically shows remaining dose in the stratum corneum. However, since there is no stratum corneum in the SynDaver skin minimal amounts were expected to be recovered from the tape strips. The lack of a lipid matrix means that the SynDaver skin model cannot act as a reservoir for chemicals during absorption. Similar to the tape strips, minimal amounts of NAP and PHEN recovered from the SynDaver skin, OPP had slightly greater amounts remaining in the SynDaver skin 2.7 \pm 2.4% dose. The lack of a hierarchical structure to provide a repeatable barrier like the stratum corneum is a main reason there have been very few synthetic skin models capable of replicating the absorption of biological skin models. However, the limitations of SynDaver skin can be overcome by creating a mathematical model.

5.4. Conclusions

While there are several surrogate materials used to simulate properties of human skin, few of them have the physical resistance crucial to represent in wipe testing and chemical absorption capabilities. The absorption of naphthalene, phenanthrene, and orthophenylphenol shows that SynDaver skin model is capable of chemical absorption. The lack of absorption of benzo[a]pyrene in both the porcine skin and SynDaver skin models indicates that the artificial sweat dosing vehicle was incompatible with benzo[a]pyrene. The lack of barrier properties and other biological skin model characteristics resulted in the SynDaver skin being more permeable than porcine skin. Although the SynDaver skin model is a simpler model relative to biological skin models, it is capable of absorbing chemicals in a similar manner. The absorption of naphthalene, phenanthrene, and orthophenylphenol generally follow the same absorptive trends in the SynDaver skin model and porcine skin model.

To further the correlation between SynDaver skin and porcine skin, additional common skin penetrants and fireground contaminants and different vehicles should be tested. This study primarily tested the absorption of PAHs, to further expand the comparisons between SynDaver and porcine skin other known skin penetrating chemicals should be tested, including caffeine, nicotine, and testosterone. Firefighters and fire investigators frequently work the fireground after the fire has been extinguished. During this stage of the fire gaseous and vapor exposures are to be expected. During overhaul phases volatile organic compounds (VOCs) have been found in high concentrations in air and biological samples. In general, VOCs have low molecular weights which indicates their potential to rapidly penetrate the skin like naphthalene. Benzene and formaldehyde would be ideal compounds for VOC absorption studies. Furthermore, these chemicals should be exposed to the skin as a vapor or gas similar to what firefighters would experience in the field.

The purpose of this study was to determine if the synthetic skin model SynDaver skin could serve as a human skin surrogate in a wipe efficacy test. The data from this study together with previous manufacturer physical property evaluations SynDaver skin would be an ideal material as a human skin surrogate for wipe efficacy testing. While the more permeable SynDaver skin may overestimate the absorption of chemicals but would be more realistic than the previous skin surrogate materials in wipe manufacturer studies.

5.5. Acknowledgements

This project was funded by Federal Emergency Management Agency (FEMA) with grant number EMW-2019-FP-00392-1 Effectiveness of Exposure Mitigation Strategies for Fire Investigators project via the Assistance to Firefighters Grant Program Fire Prevention and Safety (R&D) Grants.

Chapter 6: Decontamination Wipe Efficacy Trials on Various Surfaces

Abstract

Firefighters have started incorporating on-scene post-fire decontamination strategies to mitigate their chemical exposures during fire response, one growing strategy is cleaning the skin with decontamination wipes. Previous wipe manufacturer studies suggest that decontamination wipes are effective at removing PAHs from skin. However, the materials and methods used in previous wipe studies are not representative of the complex chemical absorption characteristics of human skin or the types of chemical exposures firefighters encounter. This study aims to replicate previous wipe manufacturer studies and modify previous methods with a more realistic human skin surrogate. Wipe efficacy testing was done with multiple commercial decontamination wipes on multiple nonporous test surfaces (polypropylene, polycarbonate, and a chemical resistant rubber) and a porous skin surrogate material (SynDaver skin). A liquid mixture of 16 PAHs was applied to the test surfaces and collected with different decontamination wipe products. The wipe effectiveness of all wipes was greater on the nonporous surfaces than the porous SynDaver skin. The average recovery of low molecular weight (MW) PAHs low (< 40% dose), most likely due to their volatile nature. Wipes were most effective at removing medium MW PAHs from both surface types. High MW PAHs had greater than 90% recovery on nonporous surfaces and drastically lower recovery, from the skin surrogate material. Low amounts of high MW weight PAHs were recovered from SynDaver skin (15% dose). No significant differences were observed across the different decontamination wipes tested ($p < 0.05$) and across the different nonporous surfaces. Wipe effectiveness for chemical removal from human skin is likely to be lower than previously suggested by wipe manufacturers.

Keywords: Polycyclic Aromatic Hydrocarbons, Decontamination Wipes, Firefighters, Dermal Absorption, On-Scene Decontamination

Highlights:

- Decontamination wipes are effective at removing PAH contamination from materials used in the firefighter turnout ensemble.
- There were no significant differences in PAH contamination removal between decontamination wipe products tested in this study.
- Decontamination wipes are likely less effective at removing PAH contamination from skin than previously suggested.

6.1. Introduction and Background

Over the past decade, there has been extensive research characterizing firefighter chemical exposures. Numerous carcinogenic chemical species have been found on the personal protective equipment, clothing, as well as on the skin of firefighters themselves [24, 47, 48, 52, 53, 174]. To reduce their chemical exposures members of the fire service industry have begun investigating different mitigation strategies such as on-scene decontamination. The goal of on-scene decontamination is to minimize chemical exposures by removing contaminants from the gear, equipment, and skin of firefighters prior to leaving the fire scene to prevent cross-contamination during transit and while living at the fire station. Depending on one's geographical location, on-scene decontamination strategies may be limited. For example, firefighters who live in northern areas of the United States and Canada may not use decontamination strategies that involve water because of the extremely low temperatures and risk of hypothermia. Generally, on-scene decontamination involves individuals setting up a wash station to clean personnel and equipment upon exiting the fire scene prior to returning to the station. Figure 42 illustrates an example of on-scene decontamination, where one firefighter is using a pressurized hose to wash a firefighter after fire response. Recent studies show that some decontamination strategies are more effective than others. Air-based decontamination ("brushing" the turnout ensemble with pressurized air) lowers contamination levels by 12 – 43%. Using a physical brush to scrub the ensemble has been shown to be much more effective, reducing contamination levels by 62 – 91%. The best decontamination method is wet-soap brushing, reducing contamination levels on the gear by 90 – 95% [47].



Figure 42: Photograph of firefighters performing on-scene decontamination.

Researchers and firefighters are growing more aware of the chemical exposures that occur on the fireground and the importance of on-scene decontamination is rapidly growing. However, even if firefighters understand the need for decontamination practices changing behavior and routine is challenging. Although the majority of firefighters' beliefs and attitudes towards clean gear are overall positive, greater than 75% of firefighters said they do not partake in field decontamination more often than "frequently," according to a 2017 Florida survey study [70]. Additionally, the use of skin wipes was the third least popular method of decontamination, whereas the most popular practice of decontamination was showering within an hour of exposure. The lack of participation in on-scene decontamination stemmed from three primary reasons: 1) firefighters are concerned about potential negative impacts on job performance from wet gear, 2) the time it takes firefighters to perform the cleaning, and 3) firefighters claimed to have higher priority problems than cleaning gear. To overcome the barriers to decontamination practices, mitigation strategies need to be simple, cost-effective, quick, and effective. Even though the use of decontamination wipes was the third least popular method of decontamination among participants in the Florida survey study, decontamination wipes are a quick and easy method of decontamination, which address two key issues. The Florida survey study was done several years ago, and since the time of the study decontamination practices may have changed as a result of new research.

Since the Florida survey study was published, several different decontamination wipe products have been introduced. However, the research on the effectiveness of decontamination wipes has not kept pace with the rate of implementation, leading to questions on which wipe would be best when considering the basic mitigation strategies needed. There is limited data currently available. Some wipe manufacturer studies boast of claims of greater than 90% effectiveness for their products, however the relevancy of the materials used in the tests is questionable [237, 184, 185]. Multiple wipe manufacturer studies used liquid contaminants in combination with non-porous surfaces as their human skin surrogate. The first issue with these materials is that non-porous surfaces do not have the same barrier properties as human skin and chemical absorption capabilities. The second issue is that liquid contaminants are not representative of the type of contaminants that firefighters encounter on the fireground. Although liquid contaminants may be easier to use in a laboratory setting, firefighters are more likely to encounter particulate matter, vapors, and gaseous chemicals on the fireground. Although there is

no standardized method to contaminate a material with vapor or gaseous chemicals, a human skin surrogate was identified in Chapter 5 that could be useful to inform future standardization.

This research is aimed at evaluating the performance of decontamination wipes at removing fireground contaminants from non-porous surfaces and SynDaver skin. This will serve to replicate the findings from previous wipe manufacturer studies and to evaluate wipe effectiveness on a material that is closer in chemical absorption and permeability to human skin. This experiment will use liquid contaminants in the same manner used in previous wipe manufacturer studies to compare the performance of the different test surfaces. The data generated from this study will be used to recommend test parameters for the development of a standardized test method to evaluate wipe efficacy for the removal of fireground contaminants from human skin.

6.2. Methodology and Materials

6.2.1. Decontamination Wipes

Currently, there are numerous decontamination wipe products available, all of which have unique ingredient combinations, fiber selection, and fabric construction. These variables may impact a wipes' ability to remove contaminants from a surface or skin, however investigation into the effects of these variables is beyond the scope of this study. Five different wipe products were selected for this study. Three products were decontamination wipes, one was baby wipes and generic dry paper towels. Different commercial wipe products were selected to determine if any wipe performed relatively better or worse than the collection evaluated. Baby wipes are a more cost-effective alternative and were selected to determine if this general, readily available product could perform as well as the commercial products. Lastly, paper towels were used as a control, a product with no additives or unique characteristics. All wipes were tested with 5 replicates in combination with each surface evaluated. Commercial wipe products were obtained through their respective websites, or they were donated by the individual company. Baby wipes and paper towels were purchased from local retail stores.

6.2.2. Surface Materials

The surface materials used in wipe manufacturer studies included a "textured board," likely to be a polypropylene product, polycarbonate, and a chemical resistant rubber. All the previously mentioned materials are used in firefighter turnout ensembles. The polypropylene, polycarbonate, and rubber materials were obtained through McMaster-Carr (Chicago, US). The

SynDaver skin surrogate, SynDaver skin basic tissue plate 2N, was obtained through the SynDaver website. Once all the materials were obtained, they were cut to provide a testing area of 10 cm × 30 cm.

6.2.3. Instrumentation

6.2.3.1. TQC Washability Tester

To conduct the wiping in a repeatable manner a TQC Scrub Abrasion and Washability Tester was used, obtained from TQC Sheen (Florida, USA). The TQC Washability Tester is used to test the resistance of finishes to scratching, wearing, and color loss due to wet or dry abrasion by simulating everyday wear through repeated motion, illustrated in Figure 43. The washability tester is compatible with several ISO, ASTM, and EN standards and was adapted to perform the wiping of the test surfaces in this study [238]. The TQC Scrub Abrasion and Washability Tester was set to 5 cycles, 20 cycles/min, and wipe length 10 cm. Wipe testing was done one at a time to minimize cross contamination, although the TQC Washability Tester is capable of testing 4 in parallel.

6.2.3.2. Buchi Speed Extractor E-916

Wipe samples were extracted via pressurized solvent extraction with a Buchi Speed Extractor E-916, seen in Figure 43, equipped with 10 mL stainless steel extraction cells. Extraction cells were prepared by placing a small cellulosic filter at the bottom of the cell before the addition of contaminated samples. Contaminated samples were rolled to fit in the extraction cell; extra care was taken by rolling the sample to not expose the gloves to contaminants, preventing cross-contamination between samples. After the samples were added to the extraction cell, a large cellulosic filter was placed at the top of the cell. Cellulose filters were added to the top and bottom of the extraction cell to prevent any debris from clogging the condensing coils of the extractor. Once all the extraction cells were loaded, they underwent extraction under the following conditions: pressure – 100 bar, temperature – 100°C, gas – nitrogen, heating phase – 2 minutes, hold phase – 5 minutes, solvent flush time – 1 minute, gas flush time – 3 minutes, solvent methanol, extraction cycles – 2. The high temperatures and pressures in the Speed extractor would melt the SynDaver skin and allow samples to be extracted via sonication. SynDaver samples were placed into a 50 mL scintillation vial along with 10 mL of methanol. Samples were then placed into the sonicator and ran for 60 minutes at 50°C. Upon completion of extraction samples were transferred to the ThermoFisher Scientific SpeedVac SPD 2030, shown

in Figure 43, and evaporated at 3.1 bar and 50°C to a volume of less than 5 mL. After evaporation, samples were reconstituted in 3 mL of methanol and vortexed. Aliquots were then taken for HPLC analysis.



Figure 43: Image of wipe test machines and analytical equipment (Top Left) TQC Washability and Abrasion Tester, (Top Right) Buchi E-916 speed extractor, (Bottom Left) ThermoFisher Scientific Speed Vac SPD 2030, and (Bottom Right) Agilent 1260 Infinity Series HPLC

6.2.3.3. High Performance Liquid Chromatography Analysis

Liquid chromatography analyses were performed on an Agilent 1260 Infinity II LC system, shown in Figure 43, coupled with Infinity Lab LC/MSD along with the following modules: Agilent 1260 Infinity Binary Pump (G1312B), Agilent 1260 Infinity Autosampler (G1392B), Agilent 1260 Infinity Diode Array Detector (G4212B) with 10 mm Max-Light flow cell (Agilent Technologies). Chromatographic separation was done using a PAH Zorbax Eclipse column (1.5 x 150mm 3 μ m pore size; Agilent Technologies). The HPLC operated under the following conditions: column temperature - 35°C; mobile phase - gradient method; 5 μ L injection volume; diode array detector was set to wavelengths 220nm, 254nm, 270nm, 285nm; fluorescence detector was set to emission λ : 425nm; excitation λ 340nm. Data were analyzed with Open Lab CDS Chemstation (Agilent Technologies). Physicochemical properties and limit of quantitation (LOQ) values for the 16 PAH compounds can be found in Table 23.

Table 23: Chemical Properties of the 16 PAH compounds used in the Wipe Tests

Compound	Molecular Weight Classification	Molecular Weight (g/mol)	Boiling Point (°C)	Vapor Pressure (mmHg @ 25°C)	logP	LOQ (ng/ μ L)
Naphthalene	Low	128.17	218	8.50e-2	3.30	0.82
Acenaphthylene	Medium	152.19	280	4.80e-3	3.94	1.01
2- Bromonaphthalene	Low	207.07	315	3.47e-3	4.2	1.00
Acenaphthene	Medium	154.20	279	2.20e-3	3.92	0.59
Fluorene	Medium	166.22	295	6.00e-4	4.18	1.01
Phenanthrene	Medium	178.23	340	1.21e-4	4.46	0.61
Anthracene	Medium	178.23	340	6.53e-6	4.45	0.80
Fluoranthene	Medium	202.26	384	9.22e-6	5.16	0.70
Pyrene	Medium	202.25	404	4.50e-6	4.88	0.72
Benz[a]anthracene	Medium	228.29	438	2.10e-7	5.76	0.65
Chrysene	Medium	228.30	448	6.23e-9	5.81	0.66
Benzo[a]pyrene	High	252.31	495	5.49e-9	6.13	0.50
Benzo[b]fluoranthene	High	252.32	481	5.00e-7	5.78	0.48
Benzo[g,h,i]perylene	High	276.33	550	1.00e-10	6.63	0.59
Dibenz[a,h]anthracene	High	278.35	524	9.55e-10	6.75	0.97
Indeno[1,2,3-c,d]pyrene	High	276.33	536	1.25e-10	6.70	0.57

6.2.4. Wipe Test Method

A 16 polycyclic aromatic hydrocarbon (PAH) stock mixture (QTM PAH MIX CRM 47930, 2000 µg/mL) was obtained from Sigma Aldrich (Missouri, USA) and was used to dope the test surfaces. The PAH stock was diluted in methanol to create a dosing solution with a concentration of 250 ng/µL. Prior to wipe testing, surfaces were cleaned with acetone and allowed to dry. The dosing solution was then used to transfer 50,000 ng of each PAH onto the surface. Following wipe manufacturer protocols the PAH mixture was allowed 60 – 120 seconds to dry and evaporate. The test surface was then transferred into the TQC Scrub and Abrasion and Washability Tester and secured into place. Once the surface was secured a wipe would be wrapped around an abrasion pad to provide a wiping area of (~ 35 cm²). Weights (500 grams) were placed on top of the abrasion pad to apply approximately 0.25psi of force was applied to the test surface during wiping. The wiping pressure used in this test falls into the wipe pressure of 0.20 – 0.40 psi recommended by Konya and coworkers for removing dirt from the skin [239]. The TQC tester was then started, wiping the surface five times back-and-forth. After the wiping was finished the wipe sample was transferred to a Buchi E-916 speed extraction cell for extraction. During trials with the SynDaver skin, the SynDaver skin was extracted via sonication.

6.2.5. Statistical Methods

Wipe efficacy or wipe effectiveness was determined by following the calculation in Equation 14. The different wipe products were compared to on another using a one-way Anova test (p<0.05). Additionally, student t-tests (p<0.05) were performed on mean values to compare if there were any effect between the nonporous surfaces and the porous SynDaver skin. During analysis values were found to be below the LOQ but above the LOD. In these circumstances values of LOQ/2 were used. The PAHs that were observed below the LOQ were marked with an asterisk in Figure 45.

$$\text{Equation 14: Wipe Effectiveness} = \frac{\text{PAH Mass Recovered}}{\text{PAH Mass Applied to Test Surface}} \times 100\%$$

6.3. Results

6.3.1. Nonporous Surface Wipe Tests

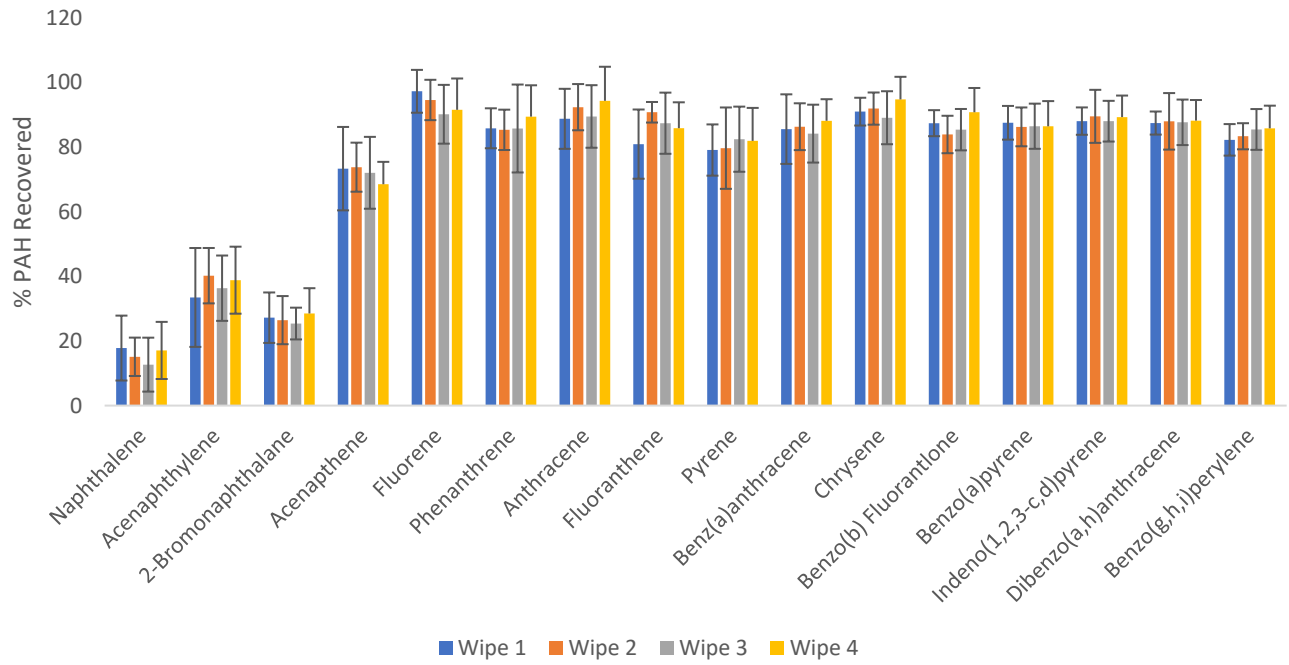
Wipe effectiveness was characterized by the amount dose of PAH that was found on the wipe after testing. Recovery of the polycyclic aromatic hydrocarbon compounds from the nonporous surfaces using different decontamination wipes were overall positive. Lower molecular weight (2 ring) compounds, naphthalene and 2-bromonaphthalene, had the lowest average recovery due to their volatile nature. Recovery of naphthalene and 2-bromonaphthalene for all wipes and nonporous surfaces ranged 7.6 – 49.1% and 16.3 – 52.5% respectively. Medium molecular weight PAHs (3 – 4 rings) excluding acenaphthylene had positive recoveries ranging 62.2 – 110.8%. The recovery of acenaphthylene ranged 33.4 – 75.1%. Lastly high molecular weight PAHs (5+ rings) had the highest average recovery across all wipe and surface combinations ranging 81.9 – 111.8%. Recoveries of each PAH on all test surfaces in combination with each wipe can be seen in Figure 44.

6.3.2. Surface and Wipe Effects

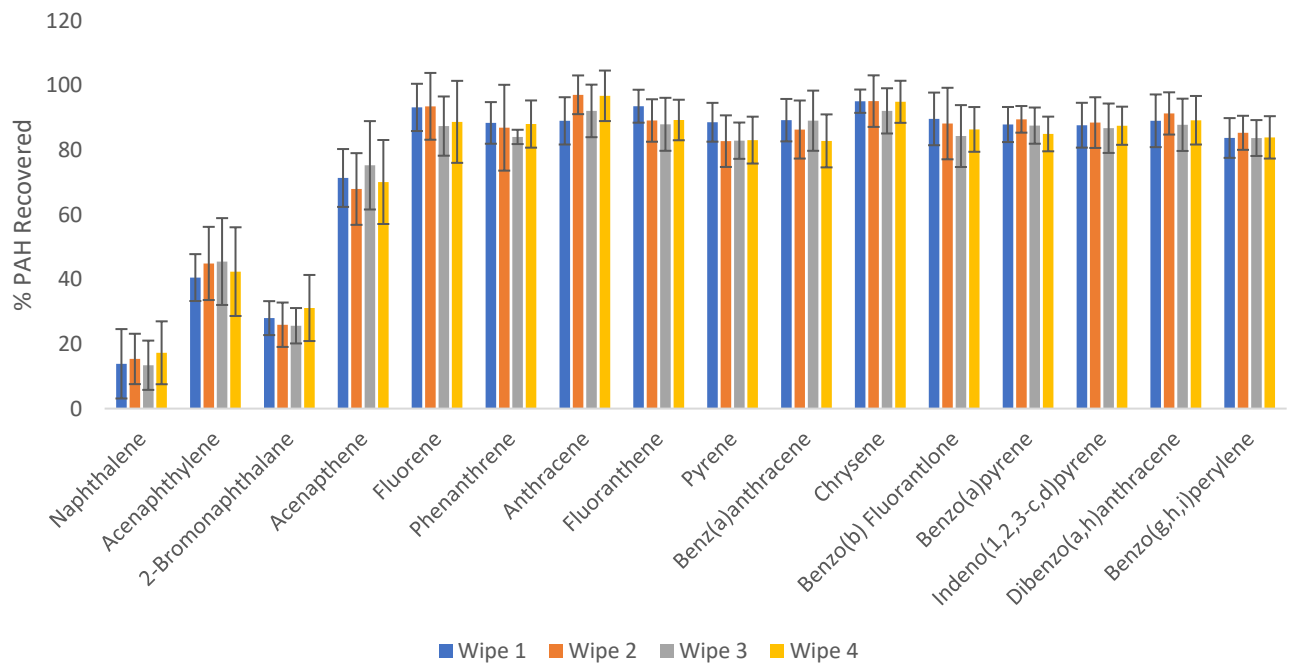
No statistical differences in PAH recovery were observed across nonporous test surfaces ($p < 0.05$), indicating no surface effects between the varied materials. The nonporous nature of the surfaces in combination with liquid contaminants is the probable cause that no surface effects were observed. The materials are designed to prevent liquid or chemical penetration, so when the liquid contaminants were applied to the surface the only solvent and some volatile PAHs evaporated, leaving the chemicals on the surface. Similarly, no statistical differences in PAH recovery were observed between the different decontamination wipe types used ($p < 0.05$), thus suggesting that the type of wipe is less important than the action wiping a contaminated surface with a clean wipe.

Figure 44: Recovery of 16 polycyclic aromatic hydrocarbon compounds from nonporous surfaces (A) polypropylene, (B) polycarbonate, and (C) rubber using 4 unique decontamination wipes.

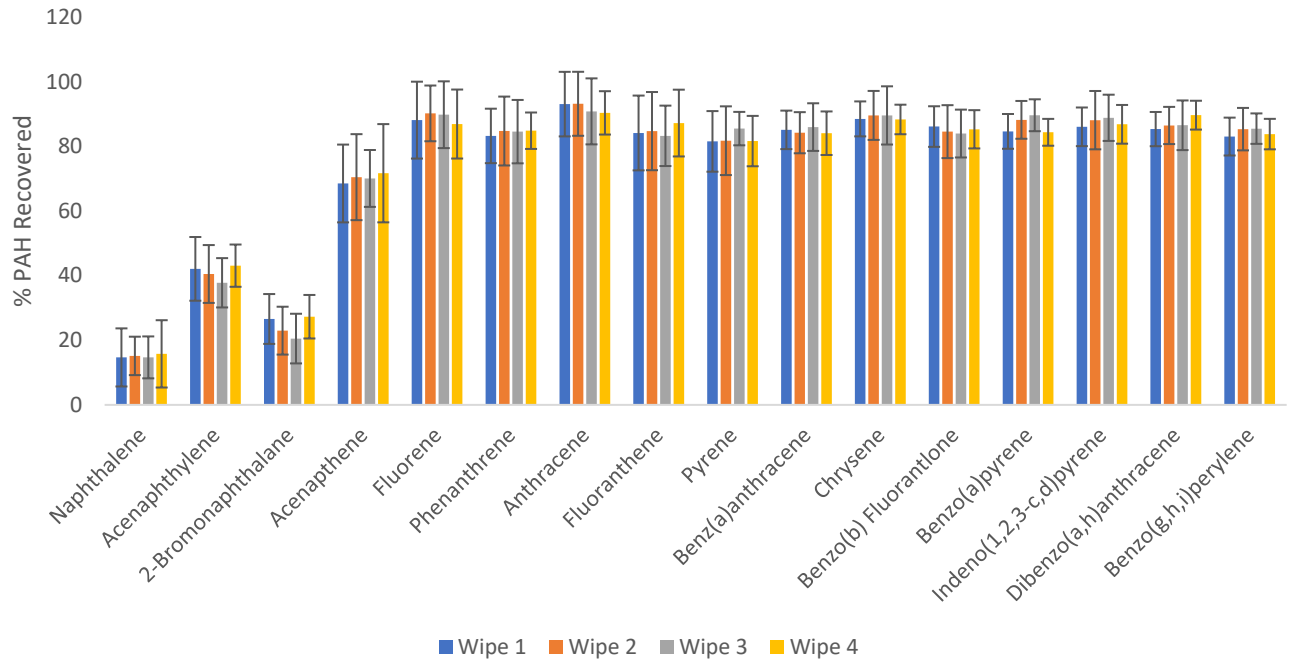
(A)



(B)



(C)



6.3.3. SynDaver Skin Wipe Tests

Wipe effectiveness was characterized by the amount dose of PAH that was found on the wipe after testing. The synthetic skin model was also extracted to determine how much of the dose was remained in the skin after wiping. In general, the wipes were less effective at removing PAH contamination from a more realistic skin surrogate such as SynDaver skin. PAH recovery in wipes and SynDaver skin is reported in Table 24. The decontamination wipes were most effective at removing the medium MW PAHs from the SynDaver skin, less effective for high MW PAHs, and least effective for the low MW PAHs. Recovery of the volatile low MW PAHs in the wipes ranged 3 – 10% in the wipes and 7 – 18% in the SynDaver skin. Medium MW PAH recovery was higher in both the wipes and SynDaver skin, 10 – 37% and 54 – 75% respectively. Lastly, recovery of high MW PAHs was lower than medium MW PAHs, ranging 3 – 15%, but higher in the SynDaver skin ranging 71 – 84%. Figure 45 shows the PAH recovery from wipes and SynDaver skin during the wipe testing.

Anova tests showed no significant differences were observed in PAH recovery across the various decontamination wipes used ($p < 0.05$). However, student t-tests performed across individual wipes revealed significant differences in removal for acenaphthylene between wipes 4 and 5, fluoranthene between wipes 3 and 5, pyrene between wipes 1 and 5 as well as wipes 2 and 5, benzo[b]fluoranthene between wipes 3 and 5, and benzo[g,h,i]perylene between wipes 1 and 5. In general, wipe 5, the paper towel, was less effective at PAH contamination removal than the other wipes. Significant differences in PAH recovery were observed between the low MW PAHs vs the medium MW PAHs ($p < 0.05$), as well as between the medium MW PAHs and the high MW PAHs. Recovery of medium MW PAHs (excluding acenaphthylene) ($p < 0.05$) and high MW PAHs ($p < 0.05$) were significantly different when wiping nonporous surfaces and the porous SynDaver skin. The difference in PAH recovery using decontamination across nonporous and porous surfaces highlights the importance of material selection for wipe efficacy testing.

The volatile nature and low recovery of low MW PAHs has been repeatedly shown throughout previous chapters and suggest that inhalation exposure is more susceptible to low MW PAH exposure than dermal absorption. However, absorption of low MW PAHs in gas phase needs to be investigated as firefighters are exposed to several volatile organic compounds found in the gas phase.

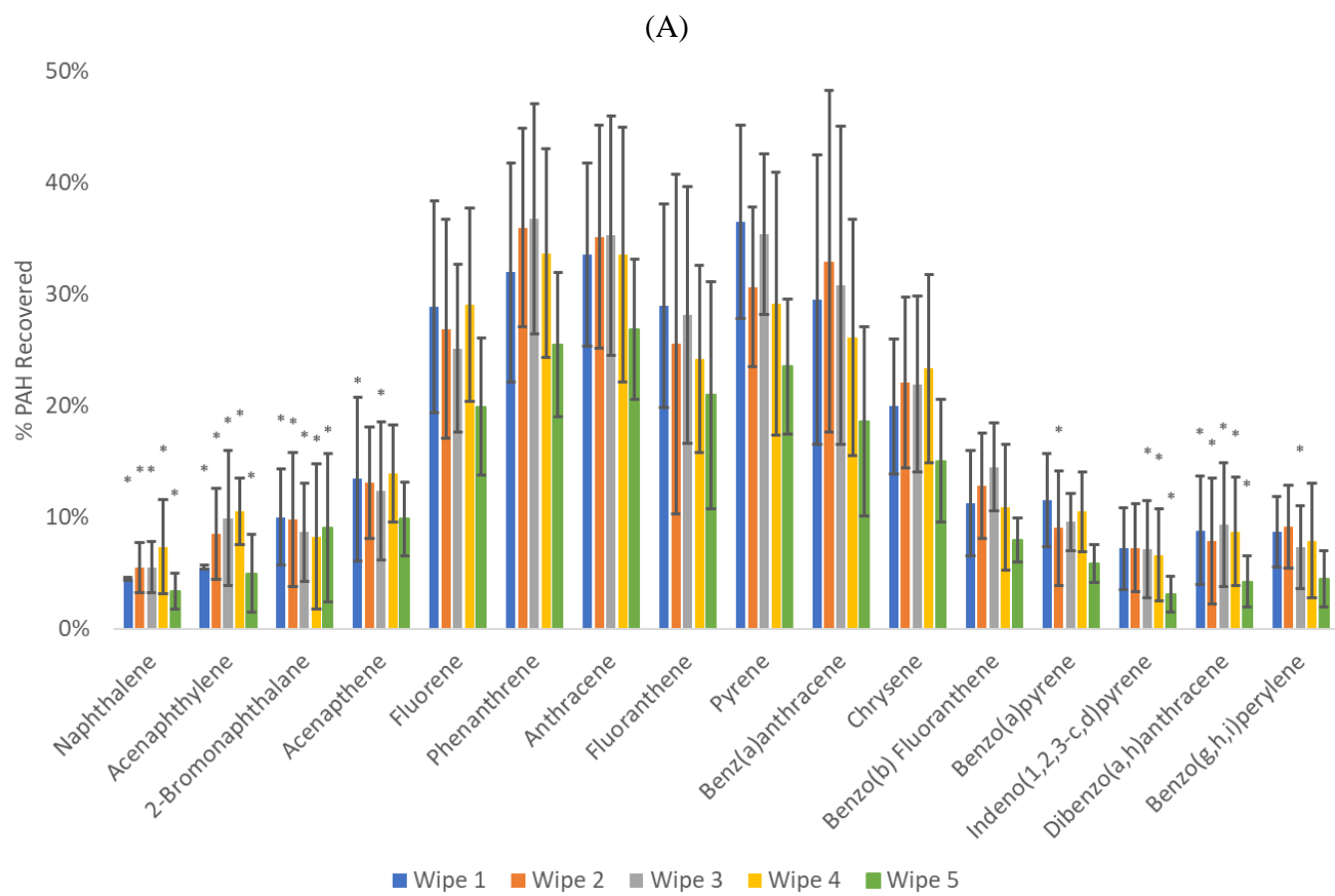
Table 24: PAH recovery (% dose average \pm standard deviation) during wipe trials with SynDaver skin

PAH	Wipe 1	Wipe 2	Wipe 3	Wipe 4	Wipe 5
Naphthalene*	4.5 \pm 0.1	5.5 \pm 2.3	5.5 \pm 2.3	7.4 \pm 4.2	3.4 \pm 1.6
Acenaphthylene*	5.5 \pm 0.2	8.5 \pm 4.1	9.9 \pm 6.1	10.5 \pm 3.0	5.0 \pm 3.5
2-Bromonaphthalene*	10.0 \pm 4.3	9.8 \pm 6.0	8.6 \pm 4.4	8.3 \pm 6.5	9.1 \pm 6.6
Acenaphthene	13.4 \pm 7.3	13.1 \pm 5.0	12.3 \pm 6.2	13.9 \pm 4.4	9.9 \pm 3.3
Fluorene	28.9 \pm 9.5	26.9 \pm 9.8	25.1 \pm 7.5	29.1 \pm 8.7	19.9 \pm 6.1
Phenanthrene	31.9 \pm 9.8	35.9 \pm 8.9	36.7 \pm 10.3	33.6 \pm 9.4	25.5 \pm 6.5
Anthracene	33.5 \pm 8.2	35.1 \pm 10.0	35.2 \pm 10.7	33.5 \pm 11.4	26.8 \pm 6.3
Fluoranthene	28.9 \pm 9.1	25.5 \pm 15.2	28.2 \pm 11.5	24.2 \pm 8.4	20.9 \pm 10.2
Pyrene	36.4 \pm 8.7	30.6 \pm 7.2	35.4 \pm 7.2	29.1 \pm 11.8	23.5 \pm 6.0
Benz[a]anthracene	29.5 \pm 13.0	32.9 \pm 15.3	30.8 \pm 14.3	26.1 \pm 10.6	18.6 \pm 8.5
Chrysene	19.9 \pm 6.1	22.1 \pm 7.6	21.9 \pm 7.9	23.3 \pm 8.4	15.0 \pm 5.5
Benzo[b]fluoranthene	11.3 \pm 4.7	12.8 \pm 4.8	14.5 \pm 3.9	10.9 \pm 5.6	8.0 \pm 2.0
Benzo[a]pyrene*	11.6 \pm 4.2	9.0 \pm 5.1	9.6 \pm 2.6	10.5 \pm 3.6	5.9 \pm 1.7
Indeno[1,2,3-c,d]pyrene*	7.2 \pm 3.7	7.3 \pm 3.9	7.1 \pm 4.3	6.6 \pm 4.1	3.1 \pm 1.6
Dibenzo[a,h]anthracene*	8.8 \pm 4.9	7.9 \pm 5.6	9.3 \pm 5.6	8.7 \pm 4.8	4.2 \pm 2.3
Benzo[g,h,i]perylene*	8.7 \pm 3.2	9.2 \pm 3.7	7.3 \pm 3.7	7.9 \pm 5.1	4.5 \pm 2.5

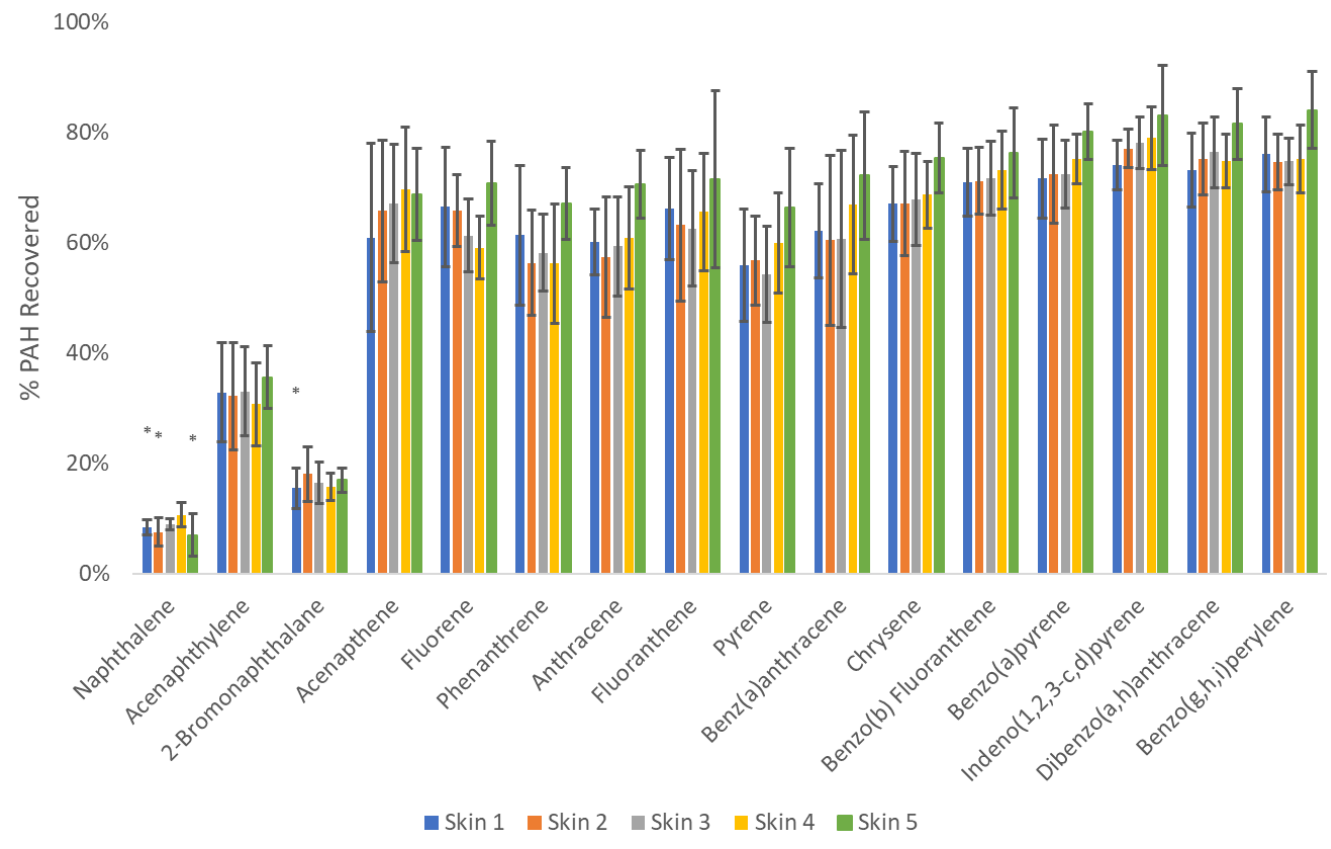
Table 24
(continued)

PAH	Skin 1	Skin 2	Skin 3	Skin 4	Skin 5
Naphthalene*	8.4 ± 1.3	7.5 ± 2.6	9.0 ± 1.0	10.7 ± 2.2	7.0 ± 3.8
Acenaphthylene*	32.8 ± 9.0	32.2 ± 9.8	33.0 ± 8.1	30.7 ± 7.5	35.6 ± 5.7
2-Bromonaphthalene*	15.5 ± 3.7	18.1 ± 5.0	16.4 ± 3.8	15.8 ± 2.5	17.0 ± 2.2
Acenaphthene	60.9 ± 17.0	65.7 ± 12.8	67.2 ± 10.7	69.7 ± 11.3	68.7 ± 8.4
Fluorene	66.5 ± 10.8	65.8 ± 6.5	61.3 ± 6.6	59.1 ± 5.6	70.7 ± 7.6
Phenanthrene	61.4 ± 12.7	56.3 ± 9.5	58.2 ± 7.0	56.2 ± 10.8	67.1 ± 6.5
Anthracene	60.1 ± 5.9	57.4 ± 10.9	59.3 ± 8.9	60.8 ± 9.2	70.6 ± 6.1
Fluoranthene	66.1 ± 9.2	63.2 ± 13.8	62.5 ± 10.4	65.5 ± 10.6	71.5 ± 16.1
Pyrene	55.9 ± 10.2	56.7 ± 8.0	54.2 ± 8.7	60.0 ± 9.1	66.3 ± 10.7
Benz[a]anthracene	62.1 ± 8.6	60.4 ± 15.5	60.6 ± 16.1	66.9 ± 12.5	72.1 ± 11.5
Chrysene	67.1 ± 6.8	67.1 ± 9.4	67.9 ± 8.3	68.6 ± 6.0	75.4 ± 6.3
Benzo[b]fluoranthene	70.9 ± 6.1	71.2 ± 6.0	71.6 ± 6.7	73.1 ± 7.0	76.3 ± 8.2
Benzo[a]pyrene*	71.6 ± 7.2	72.5 ± 8.9	72.4 ± 6.1	75.2 ± 4.5	80.1 ± 5.1
Indeno[1,2,3-c,d]pyrene*	74.0 ± 4.5	77.1 ± 3.5	78.1 ± 4.7	79.0 ± 5.7	83.0 ± 9.1
Dibenzo[a,h]anthracene*	73.1 ± 6.7	75.1 ± 6.5	76.4 ± 6.4	74.8 ± 4.9	81.5 ± 6.4
Benzo[g,h,i]perylene*	76.0 ± 6.9	74.7 ± 5.0	74.7 ± 4.3	75.2 ± 6.1	84.0 ± 7.0
*Indicates that there were some samples that were detected above the LOD but below the LOQ. In these cases, a value of LOQ/2 was used.					

Figure 45: Percent recovery of the 16 PAHs in decontamination swipes (A) and SynDaver skin (B) during wipe efficacy tests.



(B)



6.4. Discussion

The nonporous surfaces used in this study, polypropylene, polycarbonate, and a chemical resistant rubber are all materials that have been used in previous wipe manufacturer studies and used in modern firefighter turnout ensembles, specifically the facemask. These materials are intended to provide protection against liquids and vapors so that firefighters may breathe fresh air via their self-contained breathing apparatus. To provide adequate respiratory protection these materials are required to prevent any liquid or vapor penetration into the facemask. These inherent characteristics consequently make these materials unrepresentative of human skin when used in wipe efficacy testing.

Nonporous surfaces are routinely cleaned through chemical, physical, or thermal mechanisms, where wipes often utilize the first two strategies. When a nonporous material is used in conjunction with liquid contaminants, as in this study and previous wipe efficacy studies, the contaminants have no ability to penetrate the test surface. The solvent may evaporate but the chemicals remain on the surface, making it significantly easier for them to be removed by a wipe. This combination of materials and contaminants inflates wipe effectiveness. Wiping a surface has been shown to be one of the most effective methods to physically remove contamination from a surface and has been used to sample for several classes of chemicals including pesticides, flame retardants, perfluoroalkyl substances, and PAHs [162, 163, 164, 165, 168]. However, wipe effectiveness at removing contaminants from human skin is less effective, as shown in this study.

At the time of writing this, there have been two wipe manufacturers to publish data on the effectiveness of their decontamination wipes at removing contaminants [183, 185]. The first study used a “textured board that closely models the ridges and lines seen on the surface of the skin” and generated recovery values of 64 – 78% at low concentrations and 76 - 91% at high concentrations (concentration amounts were never specified). Similarly, in the second study, positive recovery rates for PAHs and chlorinated dioxins of 90% or greater were reported when wiping polypropylene, polycarbonate, rubber, and a “skin” material (no further information was provided). Both wipe manufacturers concluded that their wipes were effective at removing PAH contaminants from skin. Dose concentrations were not reported in either study, making direct comparisons difficult. As reported in the first wipe manufacturer study, concentration may influence wipe effectiveness. The dose in this study was approximately 170 ng/cm² based on

PAH mass applied and wiping area. The dose in this study is likely to be higher than the dose concentration in the second wipe manufacturer study based on dose volumes and product information, however the sampling area was never reported so there remains to be uncertainty.

Differences in PAH recovery were observed between the two wipe manufacturer studies and the results from this study. One difference that may explain the discrepancy in contaminant recovery is the nature of the surface material used to simulate skin. Although both studies used nonporous surfaces, the first study used a “textured material” that reduces contact between wipe and surface, likely resulting in lower recoveries. Whereas in the second study nonporous surfaces were assumed to be smooth, thus increasing contact between wipe and the surface, conversely inflating recovery values. The SynDaver skin is a step closer to human skin compared to the textured board and nonporous materials used in the wipe manufacturer studies. SynDaver skin has been shown to have similar physical properties as well as similar chemical absorption properties previously discussed in Chapter 5. The results from this study show that PAH recovery using a wipe was lower from the SynDaver skin than the textured board.

Human skin is the largest organ of the human body, which acts as a barrier to the environment. The skin’s primary barrier is the stratum corneum (SC), composed of dead cells called corneocytes surrounded by a lipid-rich matrix, arranged in a similar manner to a brick wall where the corneocytes analogous to bricks, and the lipid-rich matrix analogous to mortar [77]. The cellular and lipid compartments impart both lipophilic and hydrophilic properties creating an effective barrier against a wide range of chemicals; however, the SC barrier is not perfect and will allow penetration. Lipophilic chemicals are known to have a greater tendency to penetrate the skin due to easier navigation of the lipid matrix. Additionally, some anatomical regions of the body are more susceptible to chemical absorption [103, 121, 122]. Although SynDaver skin lacks the same barrier function it does absorb chemicals in a similar fashion to skin. The other surrogate materials do not have any absorption capability and should not be used to assess wipe effectiveness on human skin. Rather nonporous materials could be used to evaluate wipe construction or fiber selection on wipe effectiveness.

In the wipe tests with the SynDaver skin there were noticeable differences PAH recovery. The lower molecular weight PAHs had the lowest amount of recovery. The volatile nature of these compounds imply that they may volatilize from the surface before they can penetrate the skin. The high molecular weight PAHs had lower recovery relative to the medium molecular

weight PAHs. Unlike the low molecular weight PAHs, the high molecular weight PAHs are unlikely to volatilize. The high molecular weight PAHs are much more lipophilic and would have a high affinity for the skin rather than the wipe. The medium molecular weight PAHs are less likely to volatilize than the low molecular weight PAHs and less lipophilic than the high molecular weight PAHs. This goldilocks competing scenario regarding volatility and lipophilicity may be the reason for the high recovery of the medium molecular weight PAHs.

Although wipe sampling has been used to determine PAH contamination on the skin these values may be under representative of true contamination levels. Boeniger and colleagues (2008) tested Whatman and Alpha wipes ability to recover pyrene (medium MW PAH) from the skin. Even with the addition of corn oil as a collection media recovery of pyrene after three consecutive passes was 69% for Whatman wipes and 54% for Alpha wipes [170]. Furthermore, Keir et al. (2023) showed that decontamination wipes are not effective at reducing internal PAH dose during firefighting training exercises. Commercial wipe products were able to remove PAHs from skin, but pre- and post-decontamination concentrations were not significantly different from the control group, individuals who used no decontamination wipe. The detergent + water decontamination method was the most effective, but this method was also unable to reduce the internal PAH dose [240]. Other studies such as Fent et al. (2017) have shown soap and water decontamination to be the most effective strategy at removing PAH contamination [47]. The micelles of the soap likely collect the particulate matter and mobilize other contaminants allowing them to be easily removed with water. The lack of internal PAH dose reduction demonstrated in the Keir et al. (2023) study suggests that dermal absorption may occur during fire response, before firefighters are able to perform on-scene decontamination, or perhaps the firefighters were exposed through inhalation rather than dermal absorption. The results from this study further suggest that wipes may not be able to remove contaminants that have already penetrated the skin and only remove surface level contamination.

Although the results from this study indicate that decontamination wipes may be less effective at removing PAH contamination from human skin than previously thought, it does not mean that firefighters should discontinue using decontamination wipes after fire exposure. Removing any contaminants from the skin would be beneficial for reducing firefighter exposures. Soap has been shown by multiple studies to be an effective cleaner of both skin and

turnout gear. Wipe manufacturers may include more surfactant ingredients into wipe products to increase their effectiveness.

6.5. Conclusion

Previous studies have suggested that decontamination wipes are effective at removing PAH contamination from skin. However, the studies that originally made these claims used materials that are unable to mimic the barrier functions of human skin. When nonporous materials and liquid chemicals are used to assess wipe efficacy, the effectiveness will be inherently inflated due to the nature and interaction of the materials. Although SynDaver skin lacks the same barrier function as human skin it has been shown to absorb PAH contaminants like porcine skin. When a porous material like SynDaver skin was used to assess wipe efficacy, the overall effectiveness of decontamination wipes was reduced. The data generated from previous wipe studies that used nonporous materials should be observed as a maximum effectiveness for contamination removal.

Although the results of this study indicate that decontamination wipes are less effective than previously thought it does not mean that firefighters should not discontinue using them. Removal of any chemicals from the skin after fire exposure would reduce their potential for prolonged exposure and cross contamination. The effectiveness of decontamination wipes may be improved by changing the ingredients used in the wipes. It is likely that multiple decontamination strategies are needed to be used together to maximize the reduction of fireground contamination. On-scene decontamination is still relatively new and further research is needed on their effectiveness of removing contamination from the skin, gear, and equipment.

The liquid contaminants used in this study and previous wipe manufacturers are not the typical exposures fire responders would encounter. Rather, inhalation of toxic vapors and particulate deposition on the gear and skin is much more likely than to encounter pure chemicals. High molecular weight PAHs, such as benzo[a]pyrene, are more likely to be in the particulate phase than vapor phase like low molecular weight PAHs. The phase of the chemical changes the most likely route of exposure as well as mitigation strategies for removing the chemical. The role of the particles in firefighter exposures and decontamination has yet to be studied. Decontamination wipes have several mechanisms at removing particulate matter from a surface such as 1, 2, 3. Consequently, wipes are likely more effective at removing particulate contamination than liquid.

Currently, there is no standardized method of contamination that uses particulates that has been used to simulate fire exposure. Developing a standardized particle contamination method to simulate fire exposure would be valuable to obtain more realistic data on cleaning strategies and exposures. Additionally, repeating this experiment with particulate contaminants to assess decontamination wipe effectiveness is warranted.

6.6. Acknowledgements

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Chapter 7: Conclusions and Recommendations for a Standardized Wipe Test Method

7.1. General Summary of Work

During the summer of 2022, the International Agency for Research on Cancer (IARC) classified occupational firefighting as a class 1 carcinogen (known carcinogen). Ever since, the fire service industry has put a significant amount of time and resources towards better understanding firefighter and fire investigator exposures. Academic researchers, industry manufacturers, and fire research institutions have partnered together to conduct research on chemical exposures during fire training exercises, post-fire activities, overhaul, and life at the fire station. Numerous studies have confirmed the presence of carcinogenic contaminants in the smoke and soot, on the gear and skin of firefighters after fire response, investigated decontamination strategy effectiveness, and exposures while at the fire station. Although considerable progress has been made in recent decades, more research is needed, specifically in understanding the dermal absorption of fireground contaminants.

Even when firefighters have worn their personal protective equipment properly, fireground contaminants have been detected on their skin, making dermal absorption a primary exposure pathway. Contaminants, such as PAHs, have been found on the skin of firefighters and in biological samples. Indicating that fireground contaminants penetrate the skin during or after fire response. The difficulty in assessing firefighter dermal exposures lies in understanding the rate of absorption of contaminants and if they can be removed from the skin before they are absorbed.

This research aimed to address this gap by conducting chemical absorption studies of different PAHs *in vitro* in porcine skin and a synthetic skin surrogate using a flow through diffusion cell system. Additionally, wipe efficacy tests were done with a skin surrogate more analogous to human skin than the materials used in previous wipe studies. The information obtained from these experiments would serve to improve the understanding of firefighter dermal exposures and the effectiveness of decontamination wipes as an exposure reducing strategy.

7.2. Chapter 3: Percutaneous Absorption of Naphthalene, Phenanthrene, Benzo[a]pyrene, and Orthophenylphenol in the Porcine Skin Model

Chapter 3 tested the penetration capabilities of three different PAH compounds, naphthalene, phenanthrene, and benzo[a]pyrene, using an artificial sweat vehicle. An organic solvent is more commonly used as a dose vehicle in chemical absorption experiments, but this experiment selected an artificial sweat as the vehicle to understand chemical absorption of firefighters skin, which is most likely to be covered in sweat during fire response. The PAH compounds were tested *in vitro* with porcine skin using a flow through diffusion cell system.

The results from the PAH absorption study in Chapter 3 demonstrated that low molecular weight PAHs readily penetrate the skin even when covered in sweat. Naphthalene readily penetrated the skin, having the shortest lag time, greatest amount of dose absorbed ($34.9 \pm 4.6\%$ dose), and highest flux value (0.129 ± 0.021) ($\mu\text{g cm}^{-2} \text{hr}^{-1}$). Phenanthrene ranked in between NAP and BAP in percent dose (6.8 ± 3.2) and flux (0.102 ± 0.050). Benzo[a]pyrene had minimal amounts ($<1\%$ dose) of absorption the lowest of all chemicals tested. In general, low molecular weight compounds will penetrate the skin more readily, as seen in Chapter 03. However, the effect of sweat dose vehicle greatly impacted the absorption of more lipophilic compounds such as BAP. The high octanol-water partition coefficient and low solubility of BAP in the sweat dosing vehicle suggest that it would have a challenging time navigating the aqueous environment of the sweat to encounter the skin. As the hydrophilicity of the compounds increased absorption through the skin increased. This suggests that sweat may serve as an additional barrier and reduce the absorption of BAP and other more lipophilic compounds.

7.3. Chapter 4: Impact of the Fireground Environment on the Percutaneous Absorption of Polycyclic Aromatic Hydrocarbons

Chapter 4 was an extension of Chapter 3 and the PAH absorption experiments. These experiments aimed at understanding the effects of the fireground on the absorption of fireground contaminants. Firefighters often operate under extreme temperatures and increased skin and body temperature has been shown to increase chemical absorption. Furthermore, there is a claim that is commonly said throughout the fire service industry, which states that “for every five degrees increase in temperature there is a 400% increase in absorption.” However, there is no published study to support this claim. The first half of this experiment tested the effect of temperature and

aimed to address the validity of this “fun fact”. The absorption of phenanthrene was tested at reduced (32°C) and elevated (40°C) temperatures and compared the results to those in Chapter 3, where the temperature was 37°C. The second half of this experiment investigated if the ingredients in decontamination wipes had an adverse effect on the absorption of fireground contaminants. The ingredients of four different decontamination wipe products were added to the surface of the skin after chemical exposure. Results were compared to those in Chapter 3 to determine if any enhancement effects occurred.

Absorption and flux profiles from the temperature effect experiments indicate that there is an increase in absorption as temperature increases, although it did not extend upwards to a 400% increase. A 1.7-fold increase in flux was observed going from 32°C to 37°C and again going from 37°C to 40°C. The results from this work would suggest an approximate 70% increase in absorption. However, it is vital to consider that this increase in absorption only applies to phenanthrene and may not be applicable to other PAHs or other fireground contaminants. In general, it is difficult to make broad statements such as the one previously mentioned. Numerous factors such as environmental, biological, and fire response duties may increase or decrease dermal absorption. Although it may be nearly impossible to prevent an increase in skin and core body temperature during fire response it would be advantageous to monitor or limit a firefighter’s time operating inside a structure.

The absorption profiles from the wipe ingredients experiment suggests that decontamination wipes do not increase the absorption of fireground contaminants. However, there are limitations to the conclusions that may be drawn. The decreased absorption may be a result of how the experiment was conducted. After 15 minutes the wipe solution was added to the cell chamber and occluded for the remainder of the experiment. The addition of the wipe solution may have diluted the concentration of phenanthrene on the surface of the skin, resulting in decreased absorption. Conversely, this would support a mitigation practice of having firefighters showering within the hour after fire response to thoroughly wash fireground contaminants from the skin. The application of water on the skin would decrease the absorption of any contaminants that are on the skin by dilution or removal from the skin.

7.4. Chapter 5: Chemical Absorption Comparison of a Synthetic Skin Model to Porcine Skin

Replicating a characteristic of human skin with a surrogate material has been done for sweating, physical resistance, thermal conductivity, and several others. Replicating the chemical absorption of human skin with a surrogate skin model has yet to be accomplished. The goal of these synthetic skin models is to replace the need for animal skin models for chemical absorption studies. Unfortunately, many surrogate models have not been able to serve as a full replacement for animal skin models. However, some have been shown to potentially serve as screening model for assessing absorption characteristics of drugs and chemical compounds.

Most surrogate materials are extremely specialized and focus on mimicking a single aspect of human skin, such as chemical absorption. This work aimed to identify a human skin surrogate that had similar physical characteristics to human skin and could be evaluated for its chemical absorption capabilities. Multiple surrogate materials were evaluated and ultimately SynDaver skin was selected for further testing. The SynDaver skin model had been previously shown to have similar physical properties to human skin and similar resistance profile. Flow through diffusion cell experiments were conducted to compare the absorption of three PAHs and one fungicide in the SynDaver skin model and porcine skin.

The results in Chapter 05 demonstrated that SynDaver skin was more permeable to study chemicals than porcine skin. Although the SynDaver skin would estimate greater absorption relative to porcine skin, the absorption profiles show that the absorption was similar. After positive results from the chemical absorption studies the SynDaver skin was approved for use in wipe testing.

7.5. Chapter 6: Decontamination Wipe Efficacy Trials on Various Surfaces

To mitigate their exposures firefighters have begun implementing various on-scene decontamination strategies. One of those strategies is using decontamination wipes. This strategy is extremely simple and has few barriers to implementation. Upon exiting the fire scene and after removing their gear firefighters would clean their skin with one or multiple wipe(s), wiping the most susceptible areas of chemical deposition. Although there are several decontamination wipe products there is little data on the effectiveness of the wipes. Only two wipe manufacturers have published data on the efficacy of their wipes. However, the materials used to simulate human

skin are not the most relevant. Both wipe studies used nonporous surfaces to represent human skin and when used in combination with liquid contaminants the recovery was likely inflated. Both studies concluded that their wipes were effective at removing contaminants from human skin, but the materials used in their tests fail to incorporate the absorptive properties of human skin.

This work repeated the work done in the wipe studies while also including the SynDaver skin material to investigate if decontamination wipes are just as effective. Results show that the wipe effectiveness was significantly higher when used on nonporous materials such as the ones used in previous wipe studies. However, wipe effectiveness decreased when used on SynDaver skin. The recovery values reported from the previous wipe studies should be viewed as a best-case scenario as the nonporous materials used in those studies would provide the optimal scenario to maximize recovery. Firefighters should understand that they may not be able to remove all contaminants on their skin by simply using a decontamination wipe. Multiple mitigation strategies may be necessary to remove all chemicals present on the skin.

7.6. Recommendations for a Standardized Wipe Test Method

There are numerous wipe standards for the removal or collection of various contaminants from multiple surface types. For example, *ASTM E1792 – Standard Specification for Wipe Sampling Materials for Lead in Surface Dust*, *ASTM D6661 – Standard Practice for Field Collection of Organic Compounds from Surfaces Using Wipe Sampling*, *ISO 7503-2 Measurement of Radioactivity Measurement and Evaluation of Surface Contamination Test Method Using Wipe-Test Samples*. In addition to the large standards organization methods, there are methods published by individual researchers such as the wipe method for dermal exposures to by Boeniger and coworkers (2008) [170, 241, 242, 243].

Throughout this work a synthetic skin surrogate for human skin with similar physical and chemical absorption properties has been identified. Chapter 6 demonstrated that using a porous material decreased decontamination wipe effectiveness. The development of a dynamic wipe test method may be developed based on the findings presented here. The following are recommendations and considerations if a dynamic wipe test method were to be developed into a standardized test method for assessing wipe effectiveness of fireground contaminant removal from human skin.

Wiping a surface for the purpose of cleaning or removing a contaminant is a three-component issue. The first component is the surface that has been contaminated, which would be human skin in this context. The second component is the contaminant that is to be removed from the surface, this may range from gases and vapors to particulate matter and soot for fire responders. The final component is the tool used to remove the contaminant from the surface, defined as a single use or reusable wipe for this scenario.

To remove a contaminant from a surface it must overcome the surface energy and attractive forces between the surface and the contaminant, which is dependent on the properties of the surface and contaminant. Physical entrapment of particulates is likely to occur in areas of the body with high hair follicle density. There are several variables that can increase or decrease the recovery of a contaminant from the skin such as wiping pressure, wiping speed, number of passes, etc.

Wipe variables that influence collection efficiency include the fiber, wipe construction, and solvents used in the wipe [170]. Differences between wipe variables can be evaluated through testing. The following recommendations on pressure, wipe speed and number of wipes, contaminants and deposition methods will be covered.

7.6.1. Wipe Pressure

Pressure ensures contact is maintained between the wipe and surface. The physical force exerted by pressure aids in breaking the bond between the particles and the surface, making it easier to remove them. There are few studies to quantify the pressure used when people wipe their skin or when cleaning. There are general recommendations to “minimize force and friction” and to avoid vigorously rubbing the skin” to maintain skin barrier function [239, 244, 245, 246]. Even pressure should be applied across the entirety of the wipe to maximize the effectiveness of each pass. Too little pressure can result in redeposition or smearing while excessive wiping pressure can irritate or cause damage to the barrier functions of skin. Nurses applied “strong pressure” during wiping 5% of the time when administering bed baths [247]. Konya et al. (2020) found that both moderate and weak wiping pressures (0.23 – 0.27 psi and 0.45 – 0.48 psi, respectively) in combination with more wipe passes were able to effectively remove oily and aqueous dirt from skin [239, 247]. The pressure used in Chapter 6 falls in the lower bounds of the recommended pressure by Konya and coworkers. Future wipe methods should aim to use a wiping pressure of at least 0.25 – 0.50 psi for wipe efficacy testing.

7.6.2. Wipe Movement and Number of Passes

When firefighters use decontamination wipes to clean their skin the number of passes and time they spend cleaning their skin will be unique to the individual, where cleaning regimen may change based on perceived dirtiness and chemical exposure. Although there is no standardized number of passes for skin sampling methods, using multiple passes (greater than 2) is commonly practiced. Studies have shown more than 90% of contaminants are removed in the first two passes and any additional wipe passes will have diminished returns. Konya et al. (2020) recommended that if a lower wiping pressure is used, then three wipe passes can sufficiently remove dirt from skin [239]. The number of wipe passes done in Chapter 6 was 5 passes total. For a standardized wipe method, anywhere from 3 to 5 wipe passes would suffice.

The speed at which the wipe crosses the surface will also impact the removal of the contaminant. To overcome the attractive forces between contaminant and surface a greater force generated by pressure and wipe speed need to be produced. The shear rate is determined by the wiping velocity divided by the thickness of the contamination layer. It can be assumed that increasing wipe speed would increase cleaning effectiveness for each pass. However, if wipe speed is too high, other wipe factors may be impacted or cause damage to the skin. It is generally recommended to use gentle and controlled motions to limit forces which may cause irritation. Based on results from Chapter 6 a wiping speed of 5 – 10 cm/second would be recommended.

7.6.3. Contaminant Deposition

Several diverse types of chemicals and contaminants have been collected from skin using wipes ranging from pesticides, trace explosive particulates, PFAS, flame retardants, and PAHs. For the development of a standardized wipe method respective deposition methods will be required depending on the contaminant evaluated and its physical phase or transferred material. Liquid chemicals are commonly deposited directly to the surface via hand-held pipettes. However, if more control is required deposition may be done by machine, although both deposition methods are adequate. Meanwhile particulate deposition is more difficult, commonly done by hand particles may be damaged during the deposition process and also lack consistent spatial distribution. Several methods have been used to apply particulates to a surface. Solution deposition uses a solvent vehicle to apply particulates to the test surface, however when the solvent evaporates the particles are unevenly distributed with the highest concentration of particles along the edge of the solvent, resulting in the coffee ring phenomenon [180].

To apply a particulate contaminant in a more even manner dry transfer deposition would be better. A liquid suspension is deposited onto a transfer surface and allowed to dry. After drying, the contaminant forms a layer of normal size granules that can be transferred to the surface of the test substrate by rubbing, preventing the problem with liquid deposition where the analyte can settle in the openings of the substrate surface [188]. Drawbacks of the dry transfer method include a tedious process of allowing the liquid suspension to evaporate, damage to particles may occur, and excessive force during transfer may push particles into inaccessible openings. New deposition techniques focus on machine control transfer methodologies. Ink jet printing can deposit droplets 1 – 100µm in diameter with extreme precision, reliably and consistently. This method has been utilized to apply 10 – 30 µm cyclotrimethylenetrinitramine particles 40µm ammonium nitrate particles, and 1 – 40 µm RDX particles [180, 191].

7.6.4. Potential Impact

There is a clear need for a standardized wipe test method. Not just for evaluating decontamination wipe efficacy for firefighters, but also for other industries, for example trace contaminant analysis in forensics, or pesticide exposure in agricultural occupations. Additionally, a standardized wipe test method could help standardize dermal exposure assessments. The difficulties in replicating wipe pressure, repeating wipe motion, material selection, and contaminant deposition have been obstacles that have yet to be overcome. However, with the results from this work a realistic skin surrogate has been identified for the use of wipe testing. This addresses one of the major roadblocks of creating a standardized wipe test method. Until further research has been conducted addressing the remaining hurdles wipe testing parameters can be based on previous literature. Overall, a standardized wipe test method would drastically improve the understanding of decontamination strategy effectiveness for firefighters and fire investigators.

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